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The Anne MacKenzie Oration.[1]

"TO GUARD IS BETTER THAN TO HEAL."

By SIR ALFRED WEBB-JOHNSON, C.B.E., D.S.O., T.D., F.R.C.S., F.R.A.C.S. (Hon.),

Surgeon to Her Majesty Queen Mary, Surgeon to the Middlesex Hospital, Member of the Council of the Royal College of Surgeons of England.

I RECEIVED the invitation to deliver the Anne MacKenzie Oration on the very eve of my departure from England to visit Egypt and the Sudan and then India before proceeding to Australia to attend the annual meeting of the Royal Australasian College of Surgeons. When I learned that the oration was founded by Sir Colin MacKenzie as an act of filial piety to honour the revered memory of his mother, an answering chord was struck in my own heart, as it would be in that of any mother's son. It was, therefore, impossible for me to do otherwise than to cable my acceptance of the honourable task. No sooner had I accepted, however, than I realized that I would have to prepare such address as I could offer you without access to works of reference and without means of verifying facts and opinions which I might wish to quote. I became sensible of my responsibility as well as of the honour you had done me, and had doubts of my ability adequately to fulfil the pious desires of the founder of this oration.

But when I read something of Anne MacKenzie's life I felt sure that I would find inspiration to help me to pay tribute to the memory of so fine a character and to say something worthy of the affection and

[1] Delivered at the Australian Institute of Anatomy, Canberra, on March 20, 1939.

admiration in which she was held by her son. The theme of preventive medicine which Sir Colin MacKenzie chose as the subject for this oration is such an epic story, and such a leading part has been taken by the scientists, hygienists and statesmen of the British Empire, that there could be no lack of material upon which I might draw.

It might be thought that a surgeon would have little to tell you about preventive medicine; and yet on reflection it will be realized that Edward Jenner was a pupil and close friend of John Hunter, the founder of scientific surgery, and was often inspired by him, and that Jenner, followed by Pasteur and Lister, really laid the foundations of all preventive medical work which has been accomplished since their day.

And so, committed to this heavy responsibility, I set out on my travels—but under what different conditions from those that existed in Jenner's day, but a short century and a half ago! No fear of scurvy, no doubt about the date or even the hour of arrival at each stage of my travels, no question of the destination of journey's end. No voyage of discovery this, but the sailing of charted seas. One could not but recall with gratitude the work and sacrifices of the pioneers who had blazed the trail and brought such a programme as mine within the bounds of possibility.

Instead of a sailing ship with meagre and unvaried rations, probably lacking some vital food constituents, a floating hotel in which every reasonable and many an unreasonable want could be satisfied; instead of a small allowance of fresh water, an unlimited supply, not only for drinking but also for baths; instead of the tortures and discomforts of different climates, accommodation which was air-conditioned and could be warmed in cold weather and cooled in the tropics; instead of isolation, news from the world over by wireless each day or hour. The same wonderful invention made it possible for the navigators to receive directions by which they could steer the ship, even into a narrow harbour, however poor the visibility. In case of disaster it provided a means of calling for assistance. Even if the ship had to be abandoned there were motor launches which could keep the life-boats in a compact fleet and could maintain wireless communication until those anxious to help were guided to the scene of disaster.

We now take all this for granted. We also take for granted what is no less wonderful—that we can be protected from infectious diseases to which we are likely to be exposed during our travels.

With these reflections in my mind I landed in Egypt. How can one help being moved by a stay in that country whose recorded history begins from 3,500 years before Christ, a country to which we owe many elements of our present civilization and culture? It is the birthplace of agriculture, which first bound men to their homes and led to the earliest civilization; it is the birthplace of methods of working wood and stone, of the art of architecture, of the weaver's craft and of the making of linen, of the use of gold and copper, and of the manufacture of metal tools and implements; it is the country which gave us the solar calendar, the first alphabet and the art of writing. It is the country in which were made the first serious studies of medicine and surgery.

I found myself in a very cauldron of inspiration—in a country with written records starting from over fifty centuries ago, yet bearing today the imprint of modern man and modern invention, and reached by modern machines by sea or air under perfect conditions of health, comfort and safety.

At her gates is one of man's greatest achievements, the Suez Canal. On her mighty river are barrages which control the waters of the Nile, and protect the inhabitants against a return of the seven lean years of Joseph's time. As one travelled up the river into the Sudan, one thought of those who had laboured and of those who had given their lives in order to bring wise and beneficent government, with resulting prosperity, to the peoples of the upper Nile, and of how learning and happiness had followed in its train. One thought of those who, in the sweltering heat under pitiless skies, had laid the desert railway in the scorching sand at an average rate of a mile a day, and in one hectic effort at a record rate of four long miles between dawn and darkness of a single day. One realized how, in spite of trials, in spite of difficulties, in spite of bitter disappointments, galling defeats, useless sacrifices and sometimes burning shame, yet deliberately, definitely, with courage, persistence and endurance, the end had been achieved.

These and a host of other memories and reflections assail the mind on a journey such as this; but on deeper reflection it is borne in on one that these ends could have been achieved only by the hard path of experiment, research and trial, and that this has been going on for sixty million years and more. All through the ages, man, with his wonderful hands, with his still more wonderful thumbs, unique in the animal kingdom, has been a tireless maker of tools, instruments and machines, all the time inventing. Everything has had to be learnt, and could be learnt with certainty only by experiment, research and trial.

But I found more than this to inspire me. How was all this possible without protection against disease? With the sole exception of the mechanical sciences, no department of human knowledge has undergone so profound a change as the science of medicine, not only in unravelling the causes of disease, but in perfecting methods of prevention. Much as I was impressed with man's heroic achievements, his surmounting of difficulties and his attainment of victory by dogged perseverance, I could not but reflect that the story of the conquest of the hosts of death is a tale of heroism equal to that in any other field of human endeavour.

The bitter reflection is also forced on one that if the sums expended on weapons of destruction had been devoted to the improvement of housing, water supply and drainage, to the improvement of nutrition and other fundamental needs of health, and to the stamping out of plagues and pestilence, the result might have been better for mankind. If, instead of nation forcing nation to colossal expenditure on arms, and, owing to the threat of war, driving each other

to build winged vectors of destruction, an alliance could have been made to wage war on vectors of disease such as flies, fleas, bugs, lice, mosquitoes and such-like pests and vermin, how much more productive the expenditure would have been!

The actual treatment of the sick sinks into a secondary place when compared with the importance of measures for the prevention of disease.

In the Scriptures it is written: "They that are whole need not a physician, but they that are sick." There are some who hold the same view even today. But a great change has come over the attitude of medical men towards disease. From being mere agents in the recognition and treatment of disease, they now want to know the cause of disease and how to prevent it. Successful treatment can be devised without knowledge of the cause of a disease, and there are many instances of this in the history of medicine; but in order that plans for prevention of disease may be made, it is essential that the cause should be known. Prevention is our aim, for, in the words of Oliver Wendell Holmes:

> To guard is better than to heal,
> The shield is nobler than the spear.

Even in ancient Egypt there was considerable knowledge of hygiene and sanitation. The teachings in the books of Moses show what clear conception had been reached, and what research and observation there must have been, to enable such sound rules of preventive medicine to be codified and enforced.

In many fields the armies of construction or destruction have been brought to a standstill by preventible disease. The Suez Canal was constructed without serious setback from the invisible hosts of death; but the Panama Canal was delayed for a generation by disease, like many another mighty human effort of war or of peace. The angels of death were abroad in the land and men could hear the beating of a thousand wings; but little did they know that their Nemesis was carried by a gnat. The same small enemy had brought destruction to Greece and later to Rome. Little did the Greeks know that in the blood of the slaves they imported swarmed microbes that would destroy their mighty civilization. Yet so it seems it was. In the same way Rome crumbled to her fall when malaria spread through Italy and slowly sapped the strength of the people and made them an easy prey for the tribes from the forests of Germany. Now that some of the pestilences are held in check, it is difficult for us to picture their ravages of former days.

When one contemplates how our present measure of success has been achieved, it is clear that only by constant experiment, research and trial can the invisible enemies of man be brought into subjection.

In order to appreciate the steps by which the present stage has been reached it is necessary to have some knowledge of the history of medicine.

After the Egyptian era came the brilliant age of Greek history, when Hippocrates, Aristotle, Galen and their followers, working through the centuries, dug deep and made secure for all time the foundations of medicine as a science. The experimental method was established and medical research was carried on along scientific lines. It was the birth-time of anatomy and physiology and of the close study of disease by careful clinical observation. Another gift of Greek medicine was the code of medical ethics with which the name of Hippocrates will always be associated. Besides being the founder of the science of medicine, Hippocrates was the founder of the medical profession, described in the following words by Oliver Wendell Holmes:

> . . . a noble profession, which for more than two thousand years has devoted itself to the pursuit of the best earthly interests of mankind—always striving in unequal contest with the hundred-armed giant who walks in the noon-day, and sleeps not in the midnight, yet still toiling, not merely for itself and the present moment, but for the race and for the future.

Man had now an organized disciplined army to fight his deadliest enemies. The army waited for light and leadership, fresh inventions, new implements of war. Instead of light and leadership came darkness and the rule of dogma. But Greek medicine was built on sure foundations and could not die. When, after the dark ages and the long sleep of the scientific world, men returned to the teachings of Galen and the Alexandrians and followed again the infallible methods of experiment, research and trial, the forward march began once more.

With the revival of learning man's outlook on the world was changed by great astronomical and geographical discoveries. Our homeland was affected most profoundly, for instead of being on the edge of the known world, Britain found herself in the centre of the suddenly expanded globe. The history of Britain's greatness began only in the reign of Elizabeth; and whatever the glories of Britain in other fields since the hour of her greatness struck, her achievements in the world of science provide by no means her least and perhaps her greatest claim to fame for the benefits they have conferred on the human race.

The medical army was aroused. Speaking in this institute of anatomy, it is of interest to recall that the reveille was sounded by Vesalius with the revival of anatomy. The dawn was hailed by Harvey. It was this great Englishman who compelled a return to the experimental method. He exhorted men to "search and study out the secrets of Nature by way of experiment", and encouraged and stimulated them by the advice "*Dei laboribus omnia venduntur*"—"For toil the gods sell everything".

From the time of Harvey onwards medicine became more and more closely linked with the sciences. It has been said that only art has immortality; but I would place among the immortals those who have made great medical discoveries which have contributed so much to the benefit of mankind. Sir William Osler once asked Oliver Wendell Holmes (a master of medicine and of poetry) which he considered the greater—to have written "The Chambered Nautilus", his favourite poem, though he wrote it himself, or to have discovered the cause of puerperal fever. Holmes's reply was:

> I think I will not answer the question you put me. I had a savage pleasure in the essay. But in writing the poem I was filled with a better feeling—the highest state of mental exaltation and the most crystalline clairvoyance, as it seemed to me, that had ever been granted to me. There is more selfish pleasure to be had out of the poem—perhaps a nobler satisfaction from the life-saving labour.

But you cannot climb a mountain by a level road. There was much hard uphill work to be done, and during the seventeenth and eighteenth and the early part of the nineteenth centuries the foundations were laid for the detailed superstructure which we continue to erect and embellish today. Many British workers are to be numbered among those whose names will live. Newton led science along new lines; Sydenham, rightly called the English Hypocrates, led in clinical methods; Boyle in chemistry; Matthew Baillie, nephew of John Hunter, in morbid anatomy; Charles Bell in physiology.

A new spirit was breathed into surgery by the immortal John Hunter, who found it an applied art and left it a science. His watchword again was: "Don't think, try the experiment." Hunter was a great pathologist, anatomist and biologist as well as a great surgeon, and realized how much was to be learnt from comparative anatomy. His wonderful museum contained specimens from every part of the known world.

And then came Jenner, one of humanity's greatest benefactors. For centuries smallpox had been the greatest captain of death. Vaccination broke the evil spell of helplessness, shrinking and helpless resignation. Jenner is in a position by himself:

> While deathless heroes who maintain our fame,
> And add new glories to the British name,
> Around their brows unfading laurels twine;
> The civic crown, O Jenner, shall be thine.
>
> Ring's translation of Anstey's "Ode to Jenner".

At long last there was a scientific method of protection against a human scourge, evolved by careful observation and with no knowledge of bacteria or viruses, for man's chief enemy was still not in sight. The identification of the enemy and the study of the minute structure of the body in health and disease had to wait for the perfecting of the microscope. The compound microscope did not become an efficient instrument until 1830, little more than a hundred years ago. Lister's father was one of the chief contributors to its perfecting. Results soon followed, and man, long suspicious, became more and more convinced that there was something minute and tangible at work for his undoing. In 1862, just over seventy-six years ago, in the lifetime of many still alive today, proof was absolutely established. In discovering "the world of the infinitely small", as he called it, Pasteur made a new world for man, and the whole of our life today is based on Pasteur's discoveries.

The first great result of Pasteur's demonstration of the germ origin of putrefaction was Lister's discovery that suppuration of wounds was also due to germs, and that infection could be prevented by antiseptic methods.

Pasteur's next great achievement was the scientific attenuation of microbes, and from his researches have been evolved all our present methods of conferring artificial immunity by the use of vaccines and antitoxins.

Man had reached the climax in the fight. The discoveries of Pasteur and Lister have conferred benefits on humanity, so wonderful, so colossal and so immeasurable, which have directly and indirectly saved so many millions of lives, that their names stand out in letters of flame above all others in the fight to victory.

Advances were swift and sure along the paths opened up by Pasteur. The story of the conquest of the tropics is an epic, full of examples of dogged perseverance, skilful tracking of the enemy, and heroic and dauntless self-sacrifice by the searchers after truth. The result was not only to convict the enemy hosts of disease, but also to prove the blood-guiltiness of the insect hosts which acted as vectors of infection. The incidents and the results of this heroic work were achievements of the order of deeds that men write upon stone.

Malaria and yellow fever held the tropics against the white man. To Ronald Ross belongs the honour of the actual detection of the mosquito as the carrier of the malarial parasite. The pæan of praise and thanksgiving which filled his soul as he realized that the truth was revealed to him found expression in a verse which he penned the same night:

> This day relenting, God
> Hath placed within my hand
> A wondrous thing; and God
> Be praised.

Manson, whose suggestions had inspired Ronald Ross, had consignments of infected mosquitoes sent to London. Just as Jenner vaccinated his own child, so these mosquitoes were allowed to bite Manson's own son; he developed the disease and the parasites were found in his blood.

In the conquest of yellow fever eleven individuals volunteered for the crucial experiment and were bitten by mosquitoes which had previously been allowed to fill themselves with blood from yellow fever patients. Two of the volunteers contracted the disease and one fell a victim to the cause of science and humanity. It is just as wonderful that the Panama Canal was cut through a belt of malaria and yellow fever as that it divided a continent into two and linked two oceans together.

Little did early man think that his real enemies were microscopic animalcules and unicellular vegetable microbes, and that often the angels of death were insect hosts. Primitive man had to equip himself to fight the enemies visible to him. The hand and brain of modern man had now fashioned instruments and methods which brought the real enemy into view. The battle was joined, and man, instead of fighting something mysterious, had the hosts of death captive. He could study them as tiny specks on a microscope slide, or hold them encaged in a test-tube—growing at his command, tamed, attenuated, robbed of their virulence and often to be used as allies against their venomous brethren.

Thus, while there has been a revolution in other branches of life since Jenner's day, changes have taken place in the science and practice of medicine which also amount to a revolution. Many of the changes—for example, vaccination, anæsthesia and antiseptic surgery—met with opposition from both inside and outside the profession. Australians may remember with pride that Gilbee, of Melbourne, put Lister's methods into practice the same year as they

were published. Opposition to change may be a matter for reproach, but this cannot be levelled at the medical profession only; it is a common human failing. Too often a new truth has to fight its way to acceptance against unreasonable opposition, or against some fixed opinion or bias.

> Alas, what years you thus consume in vain,
> Ruled by this wretched bias of the brain.
>
> Crabbe.

Nevertheless, advances have been steady, although sometimes slow and painful. Preventive and curative methods now make us masters of many diseases. Surgery is now safe as well as painless. The tropics can be made safe for the white man. The list of diseases which we can positively prevent or cure is an ever-increasing one. The average expectation of life has been increased by several years, and thousands who are alive today would have been dead had it not been for the application of knowledge gained in the sphere of medicine.

The countries I have visited on my way here have not only filled me with admiration for some of man's greatest achievements in constructive art and in the fight against the hosts of death, but they have also made me realize that though much has indeed been done there still remains much for us to do. We are but at the beginning; or as Newbolt said: "We are like children playing on the shore of the infinite ocean of truth."

In many countries medical officers of health are faced with problems of preventive medicine which may be are greater and call for more courage and steadfastness from the very fact that the causes of infection are known and the difficulties made apparent. Nevertheless they fight steadily on, undeterred, continually applying knowledge already available and continually seeking for fresh knowledge, realizing full well that throughout the ages a golden truth is blazoned: the path of progress is by experiment, research and trial. Modern inventions themselves bring new problems and new dangers. The members of medical services now shoulder a tremendous responsibility, not only in the control and prevention of infective diseases which are endemic in their own countries and may appear at any time in epidemic form, but also in constantly guarding the inhabitants against the importation of infections from across the frontiers. This entails not only the waging of perpetual war against infective diseases and the insect carriers of infecting agents, but also the exercise of the keenest vigilance over the steady stream of aeroplanes that bring distant countries within a few hours' journey.

The advantages of rapid transit carry with them the dangers of importation of disease or of vectors of disease from countries in which such infections as cholera, yellow fever, sleeping sickness and other scourges of man and beast are endemic. Oceans and desert tracts, which formerly made effective barriers between countries and could be crossed only by sea-going ships or "ships of the desert" in several weeks, can now be traversed in a few hours by fast aeroplanes, which can even put a girdle round about the earth in a matter of days. Aspirants to record flights round the world must remember that medical officers can hold up ships at sea or in port. They must not be surprised, therefore, if they and their aeroplanes are interned if they pass rapidly from fever-stricken countries to those free from infection.

Acute diseases attract immediate attention. Their effects are dramatic; they strike terror into peoples and into armies. Winston Churchill drew a vivid picture of an outbreak of cholera which struck the army during Kitchener's advance up the Nile. Death moves continually about the ranks, silent, unnoticed; and the summons is almost ignominious.

> To find the servant dead in the camp kitchen, to catch a hurried glimpse of blanketed shapes hustled quickly to the desert on a stretcher, to hold the lantern over the grave into which a friend or comrade—alive and well six hours before—was hastily lowered, even though it was still night; and through it all to work at pressure in the solid, roaring heat, with a mind ever on the watch for the earliest of the fatal symptoms and a thirst that could only be quenched by drinking of the deadly and contaminated Nile. All these things combined to produce an experience which those who endured are unwilling to remember but unlikely to forget.

The fight against acute pestilences is quickly organized; quarantine—a word derived from the forty days' segregation against the plague introduced by the Republic of Ragusa in the fourteenth century—is imposed, and every other precaution is taken. On the protective side it is comforting to know that the efficiency of prophylactic vaccination against cholera and plague is now generally recognized, and that a vaccine for yellow fever has been tried and gives promise of success.

There is no apathy in fighting an acute pestilence, and so the slow killer is the greater danger in the end, for the effects are not immediate and death comes after a long, insidious illness. Tuberculosis is still a deadly infection, especially on virgin soil such as a native community. The scourge which the white man has carried to all lands, where he had only to cough to kill, is an abiding danger today. Yet it is well over half a century since Koch discovered the tubercle bacillus.

Malaria is still one of our most formidable enemies. It is probably the largest killer of all diseases, and the greatest single cause of disability and loss of energy. While urban districts may be kept free, what a task to control it in rural districts, when a single small stagnant puddle provides sufficient breeding ground for millions of mosquitoes!

In Egypt 80% of the population are infested with a parasitic worm of some sort—bilharzia or ankylostoma. Bilharzia takes a heavy toll of life. The cause is known; but again, what a task to prevent infection! Millions of the fellaheen, working in the irrigation channels on which Egypt's life depends, are infected through their skins by tiny worms that pass part of their life cycle in the bodies of snails which abound in the waters of the Nile. The infestation travels through the blood stream and settles in its human victims, particularly in the bladder. Successful treatment is possible in the early stages; but it is a colossal undertaking to break the life cycle of this parasite and to prevent millions of agricultural workers from reinfecting the soil. The soft waters of the Nile are indeed fateful, for they give both life and death.

All has had to be found out by research—the cause, the treatment, and how to prevent a disease; but the task of prevention is so enormous that only expenditure equal to war expenditure could finance the effort. If only peace could be ensured the terrific effort might be made.

Pestilences of war have to be controlled; otherwise in the Great War millions of men could not have been kept in the field for over four years. The cause of typhus is known and the disease can be prevented. The cause of typhoid is known and armies can be protected.

During the War I was attached as surgeon to the main typhoid hospital on the lines of communication in France. In this hospital (Boulogne Base Hospital) we saw only a few thousand cases. If the disease did occur among the inoculated it was relatively mild in character and the mortality was negligible. Yet in the South African War there were 58,000 cases and 8,000 deaths in a comparatively small army. This revolution was the achievement of Sir Almroth Wright, the originator of protective inoculation against the typhoid group of fevers. It is somewhat of a romance that during the War Sir Almroth Wright was working in an army laboratory in Boulogne and that in that same French town was a statue of Jenner inscribed with the following words:

A Edward Jenner
La France reconnaissante.

The statue was erected by a grateful people to commemorate the fact that although France and England were at war Jenner had sent his assistant, Dr. Woodville, with a supply of vaccine for the people of Paris, where a severe epidemic of smallpox was raging at the time. What a contrast to the present day, when so-called civilized nations are discussing whether their enemies are likely to shower pestilence upon them from the skies!

Progress has been made against common infections of temperate climes as well as against tropical diseases. The streptococcal infections, puerperal fever, septicæmia and erysipelas, are robbed of half their terrors since the discovery of "Prontosil". Pneumococcal and other infections respond to the chemical remedy "Dagenan" or "M. and B. 693". Specific remedies have been discovered for many infectious diseases. Immunity can be ensured against most of the common infectious fevers of childhood.

But to leave the proved infections, let us turn at the end to one of the most terrible scourges of civilized peoples today—the scourge of cancer.

With the increasing average age of populations, due to smaller birth rates, to a lower infant mortality rate and to a greater expectation of life, this terrible disease grows more and more common. Increasing thousands yearly turn to research workers and anxiously cry: "Watchman, what of the night?" Each year we feel that the dawn is nearer at hand. Though we are not yet aware of the cause, we are far from helpless in regard to treatment of the condition.

We know that in its early stages the disease is essentially a local one. Provided it is diagnosed early and provided it is accessible, we know that there is a good prospect of its complete eradication. It is necessary to rid people of their haunting dread of this disease and to induce them to seek advice without fear when their first suspicions are aroused, so that the condition can be diagnosed in its early stages and treatment undertaken with good prospect of cure.

The most intense efforts are being made to shed light on this problem. Besides clinical work, experimental work is being conducted on the filterable agents and viruses; on the intricate problems of immunity, in which results are often misleading; on the influence of heredity; on the metabolism of tumours; on cancer-producing compounds; on substances which produce growth; on the œstrogenic agents and hormones; on the mode of spread of the disease; on the combined effects of radiation and cancer-producing agents; on the physical and biological effects of X rays, radium and short wireless waves; and on the effects of neutron radiation.

This range of experimental investigation requires the labours of chemists, physicists, biologists, eugenists, physiologists and pathologists—and all of the highest order, for the real talent for research is possessed only by the few. Specialists have to be engaged on different lines of investigation, for to make progress in this complex subject specialization is imperative.

But, for the results of various researches to be applied, they must be built up into a composite whole. From the enormous accumulation of details the truth must be demonstrated by some rare genius with the faculty for seeing the hidden relations between various phenomena. Some man of genius with a wide biological outlook and creative imagination will eventually indicate the line leading to the solution of this problem.

Each year fresh hope is awakened by some new line of research. At the present time many minds are turned to neutron rays and the possibility of using artificially prepared radioactive substances of more selective action than X rays or radium, and many times more powerful.

With the remarkable machine, the cyclotron, invented by Professor Lawrence of California, neutron rays can be concentrated on a tumour, or the neutrons can be fired at various chemical atoms, and the resulting radio-active atoms may, according to their chemical composition, have a selective action on the cells of tumours in different organs or tissues. A new avenue of work is opened up. The avenue is probably long, and light may be but dimly discernible at the end; but hope is aroused and the path must be explored.

The cyclotron is an expensive apparatus, costing about £30,000. A few machines have been installed in different countries, and it is of urgent importance that full clinical trial be made, as soon as possible, of the therapeutic value of neutrons.

I say "as soon as possible" advisedly, because the time is not yet. First of all we must be sure of the physical side of the experiment. We must know that accurate dosage can be ensured. Intensive work must also be done on the biological effects of neutron radiation. Unless we start from a proper scientific foundation the clinical trial will be beset with dangers and uncertainties.

There are many medical discoveries still to be made. What today are but the visions of scientific men may one by one be turned into realities, and the conditions of human life altered more profoundly in the next five decades than in the five centuries since the Renaissance.

Progress will be maintained only by constant experiment, research and trial. If anything I have said today stimulates interest in preventive medicine and leads anyone to give support to medical research, the pious wishes of the founder of this oration will have been fulfilled and the high example set by his revered mother will not have been in vain.

CLINICAL APPLICATION OF THYREOTROPHIC HORMONE.[1]

By K. S. HARRISON,

From the Department of Medicine, University of Sydney.

THE thyreoid-stimulating principle of the anterior pituitary has been extensively investigated in animal experiments during the last nine years, and its effects are well recognized. This thyreotrophic hormone, when administered parenterally, activates the thyreoid gland, producing a condition which closely mimics human hyperthyreoidism. The thyreoid gland shows elevation of epithelium and loss of colloid, the metabolism and heart rate are increased, and there are changes in other organs which may be attributed to heightened output of thyreoid hormone.

The first report of its administration to a human patient was by Schittenhelm and Eisler[10] (1932), who gave injections of thyreotrophic hormone to a healthy girl, convalescent from apiol poisoning, and obtained a rise in basal metabolic rate and blood iodine level. A little later these investigators[11] reported the case of a patient suffering from myxœdema following thyreoidectomy, who received eight daily doses of 600 units without alteration of basal metabolic rate. Thyroxine, given later, caused a rapid rise from −30% to +30% in one week. In addition, a young obese woman treated with diet and thyreotrophic hormone lost a little weight, but exhibited no elevation of metabolic rate.

At approximately the same time Eitel and Loeser[1] (1932) described ten patients, some normal and some goitrous, three of whom they discussed in detail. Six hundred guinea-pig units of thyreotrophic hormone, injected daily for six days, produced a rise in basal metabolic rate of 20% to 30%, with swelling of the thyreoid gland, tremor, tachycardia *et cetera*.

Müller[7] (1933) treated several patients in the later months of pregnancy with 200 to 600 units of thyreotrophic hormone daily, but obtained no demonstrable effect. Feuling[4] (1933) injected 57 patients with thyreotrophic preparations, and observed an average rise in basal metabolic rate of 15% to 19% after four daily injections.

Wachstein[16] (1934) treated a female patient, aged twenty-eight years, with daily doses of 600 units of thyreotrophic hormone. After a total of 5,000 units had been given the basal metabolic rate had risen from −28% to −2%, and this rise was associated with an improvement in the clinical condition and the restoration of the menstrual flow. A second course of 3,000 units one month later evoked a smaller response, and a third course of 4,000 units produced no rise at all in basal metabolic rate. Wachstein attributes these results to the development of refractoriness, such as is seen in animals after long-continued administration of the hormone. A second patient suffering from hypophyseal cachexia, with a basal metabolic rate of −28%, failed to respond to 8,000 units, possibly because the thyreoid gland had atrophied and had become insusceptible to stimulation.

Thompson[15] (1935) described the results of the administration to twenty-eight patients of various types of thyreotrophic preparations, namely, "Phyone", of Wilson Laboratories, and "Growth Hormone", of Squibbs and Company, in doses of four to eight cubic centimetres daily. In eighteen of these patients there was obtained some increase in metabolism, which, however, was only temporary, in spite of continued administration. Some patients with previously low basal metabolic rates (−15% to −30%) exhibited a rise in rate to the normal level; but two with marked myxœdema showed no change. Again, several patients with hyperthyreoidism were made worse by the injections.

Lederer[6] (1935) reported two patients with Simmond's disease treated with "Preglandol". Their metabolic rate rose, but fell again to the previous level about three weeks after cessation of treatment.

Starr[14] (1935) gave to twenty-four patients the Parke, Davis thyreotrophic preparation "Antuitrin-T", containing approximately 50 guinea-pig units per cubic centimetre. Four normal adults exhibited a rise in basal metabolic rate of 20% to 24% after three to eight daily injections of one cubic centimetre. Four castrated women gave a similar response. One patient with myxœdema failed to react to eight daily injections, but an elevation of metabolic rate was obtained in cases of mild hypothyreoidism. Several patients showing hyperthyreoidism exhibited a further elevation of their metabolic rate, but even after very prolonged administration they did not seem to develop refractoriness or thyreoid inhibition.

It is difficult to correlate the effects produced by these small, almost homœopathic, doses of 50 units *per diem* with those described by most other workers, who give daily 600 to 1,000 guinea-pig units.

Scowen[13] (1937) treated several series of patients with thyreotrophic hormone. Normal

[1] This work has been performed during the tenure of the Marion Clare Reddall Scholarship of the University of Sydney, and as part of a research programme generously aided by a grant from the National Health and Medical Research Council to Professor C. G. Lambie.

individuals injected intramuscularly with 1,200 Heyl-Laqueur units every day for three days exhibited a prompt rise in basal metabolic rate up to +40%, with a fall to normal in two to three weeks. The low metabolic rates of three patients suffering from destruction of the pituitary gland by tumour growth were elevated by similar quantities of thyreotrophic hormone. Another man with hypothyreoidism, probably due to pituitary insufficiency, showed a marked response to 6,000 units, as evidenced by increase of basal metabolic rate up to +88%, thyreoid swelling and other manifestations of hyperthyreoidism, all of which rapidly subsided. Six cases of true myxœdema were not influenced by 6,000 units of thyreotrophic hormone, although they responded to thyroxine. Scowen concludes from this that in true myxœdema the thyreoid gland is so atrophic that it is unable to respond to thyreotrophic stimulation.

From this brief review of the literature it can be seen that the thyreotrophic hormone will raise the metabolism of normal individuals, and of those suffering from mild thyreoid insufficiency, but is ineffective in true myxœdema. Those patients who respond by an elevation of the metabolic rate may show obvious clinical improvement or even exhibit signs of mild hyperthyreoidism.

The object of the present investigation has been to correlate the effect of the thyreotrophic hormone on the basal metabolic rate with the blood cholesterol level in primary and secondary thyreoid insufficiency. As far as could be ascertained, the changes in blood cholesterol content after thyreotrophic hormone administration have not previously been followed clinically.

Experimental.

Thyreotrophic hormone was administered to five patients exhibiting different types of thyreoid insufficiency, and its effects on the basal metabolic rate, blood cholesterol, and clinical state were recorded.

Methods.

The patients were all maintained at rest in bed for some time before and during the period of study. The basal metabolism estimations were performed by the Douglas bag technique under standard conditions.

The blood for cholesterol determination was withdrawn with the patient in the fasting condition usually at the time of the basal metabolic tests. One cubic centimetre of blood was dried on filter paper and extracted continuously for one and a half hours with chloroform. The cholesterol in the extract was then estimated colorimetrically by the Liebermann-Burchardt method. The result recorded was the total cholesterol content of the whole blood. All the determinations were carried out in duplicate.

The thyreotrophic hormone,[1] comprising two batches, one containing five and the other ten Junkmann-Schoeller guinea-pig units per milligramme, was prepared for injection by being washed with alcohol and ether, dried, and dissolved under aseptic conditions in sterile saline solution. After solution each was incubated aerobically and anaerobically for forty-eight hours to test the sterility of the preparation. The dose of 1,000 units was contained in approximately four cubic centimetres of solution, and was injected intramuscularly. Four of these five patients complained of some soreness at the site of injection, but this disappeared in from twenty-four to forty-eight hours.

[1] Grateful acknowledgement is made to Professor Schoeller, of Schering A.G., Berlin, for a generous donation of this preparation to the Department of Medicine.

Results.

CASE I.—Mrs. S., aged forty-four years, suffered from a pituitary tumour. She had complained of progressive dimness of vision and weakness for three years. She was an obese woman, somewhat dull mentally; the left eye was completely blind owing to optic atrophy, while the right eye exhibited temporal hemianopia. No signs of myxœdema, such as dry skin, subcutaneous infiltrations *et cetera*, were present. The diagnosis was a tumour involving the pituitary region.

Following the administration of four daily doses of 1,000 units of the thyreotrophic hormone the metabolic rate rose from −19% to −6% and the blood cholesterol level fell from 204 milligrammes per 100 cubic centimetres to 91 milligrammes per 100 cubic centimetres of blood (Figure I). The pulse rate was irregularly increased, but there were no other clinical manifestations.

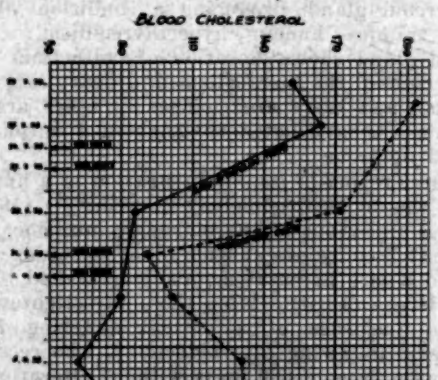

FIGURE I.

CASE II.—Miss G., aged thirty years, suffered from mild hypopituitarism. She had had amenorrhœa on and off for three years, the last period being three months before the date of examination. She also complained of weakness, lassitude and loss of weight.

She was a thin, nervous woman with no signs of hypothyreoidism. No pelvic cause was discovered for the amenorrhœa. X ray examination revealed a small inactive tuberculous lesion at the apex of the left lung.

After four daily doses of 1,000 units of thyreotrophic hormone (Figure II) the basal metabolic rate rose from about −10% to +8%. The blood cholesterol level fell from about 160 to 107 milligrammes per 100 cubic centi-

metres of blood. The maximum variation of the five control cholesterol estimations was only 29 milligrammes per 100 cubic centimetres of blood.

After the second dose of thyreotrophic hormone the patient complained of some malaise and a "sore throat". On examination, a definite, diffuse, slightly tender enlargement of the thyreoid gland was found. Slight tremor of the hands and sweating were observed. There was no sign of exophthalmos. The pulse rate was elevated to 90 per minute.

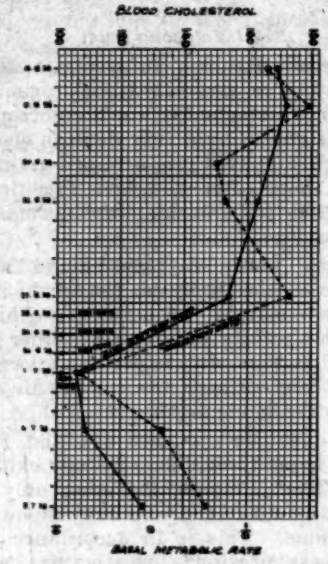

FIGURE II.

The day after the fourth injection she commenced to menstruate, the flow continuing for three days. Although no further therapy was given, the periods recurred one and two months later, lasting two days on each occasion.

The thyreoid swelling, tremor and tachycardia had completely subsided three days after the last injection. During the administration of the hormone the patient appeared a little more excitable than previously, felt less tired and was more alert.

CASE III.—Mrs. C., aged forty-two years, suffered from hypothyreoidism. She had complained of weakness and lassitude for ten years, amenorrhœa for ten years, and breathlessness on exertion for two to three years. Weight had been constant. She noticed dryness of skin and falling out of hair.

She was seen to be a pale thin woman with dry skin, some loss of hair from eyebrows and forehead, but no subcutaneous deposits nor infiltration of the tongue, lips or eyelids. Speech seemed a little thick.

The urine contained albumin, but no other abnormal constituents. Blood examination revealed a mild degee of macrocytic anæmia.

Some difficulty was experienced in obtaining satisfactory estimations of metabolic rate, as the patient had a tendency to overbreathe, with resulting high respiratory quotient, sometimes over unity. The results depicted in the graph, however, are those in which the respiratory quotient was within the range of normal variation.

There was a complete absence of response to four daily injections of 1,000 units of the thyreotrophic hormone as regards the metabolic rate, but in spite of this a definite fall in the blood cholesterol occurred from 340 to 237 milligrammes per 100 cubic centimetres of blood. Apart from this there was no clinical evidence of benefit from the administration of hormone: no elevation of pulse rate, no change in the skin, speech or sense of well-being.

With subsequent oral administration of small doses of thyreoid extract, 0·12 to 0·18 gramme (two to three grains) *per diem*, the basal metabolic rate rose to +3% in two weeks. The blood cholesterol fell even further to 141 milligrammes per 100 cubic centimetres, the skin became moister and speech clearer.

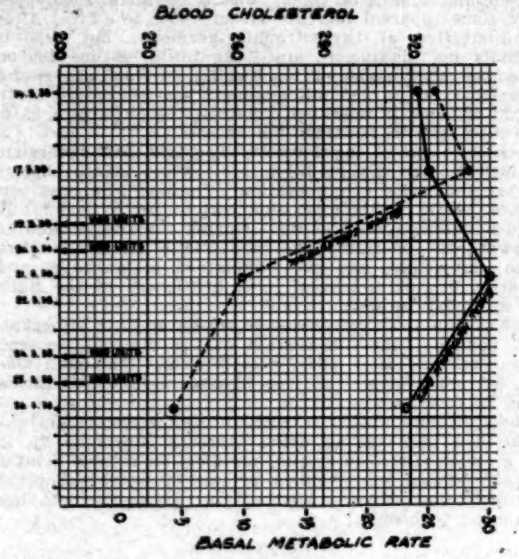

FIGURE III.

CASE IV.—Mr. A., aged fifty-eight years, suffered from myxœdema. He had complained of shortness of breath and weakness for three to four months, some swelling of the abdomen, and cough. He was found to have a typical, pasty, myxœdematous facies with infraorbital pouches, loss of hair, dry skin, infiltration of the tongue and supra-

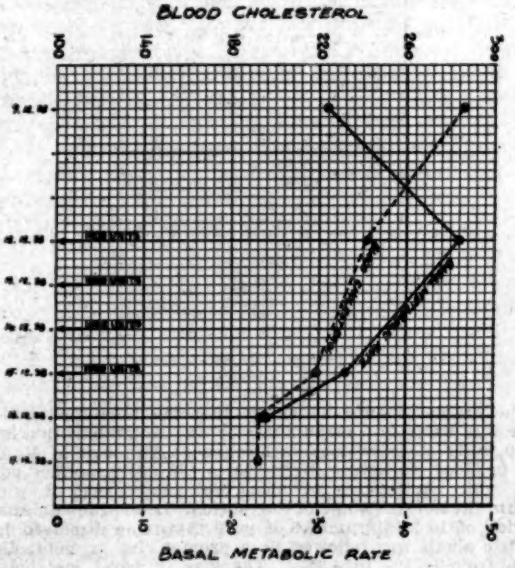

FIGURE IV.

clavicular pads. His speech was thick and monotonous. The heart was considerably enlarged. Auricular fibrillation with slow ventricular rate was present. The liver edge was palpable 2·5 centimetres (one inch) below the

costal margin, and a little fluid was detected in the abdominal cavity. The red blood cells numbered 4,030,000 per cubic millimetre; the hæmoglobin value was 78%. A test meal revealed achlorhydria.

Unfortunately this patient was too ill to be deprived of the benefit of treatment with thyreoid extract for any considerable length of time. The basal metabolism does show some apparent increase (from −46% to −24%) after administration of thyreotrophic hormone; but this is probably not significant, since the initial estimation on December 9, 1938, was −31%. The fall in blood cholesterol level from 241 to 195 milligrammes per 100 cubic centimetres of blood is small but definite. The pulse rate, skin, speech *et cetera* remained unchanged.

Case V.—Miss B., aged twenty-six years, had undergone total thyreoidectomy in July, 1937, twelve months before the present period of observation. The operation was performed by Dr. Poate upon this patient for a moderately large non-toxic colloid goitre. During the twelve months following the operation she gained 12·6 kilograms (two stone) in weight, and she complained of weakness and lethargy, dry skin, loss of hair, brittleness of the nails and a lumbar backache.

She was an obese young woman, weighing 77·75 kilograms (195 pounds); the distribution of the fat was general. Supraclavicular fatty pads were present. The skin was dry, but no evidence of true myxœdematous infiltration could be found.

Physical examination revealed no other abnormalities.

She had been taking dried thyreoid substance up to 0·84 gramme (fourteen grains) *per diem* for several months without clinical improvement or loss of weight; but the administration was stopped two weeks before her admission to hospital.

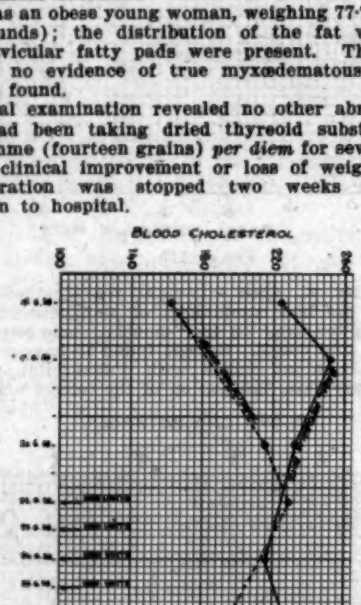

Figure V.

The graph (Figure V) shows that the basal metabolic rate was entirely uninfluenced by the administration of 4,000 units of thyreotrophic hormone. Although a slight fall in blood cholesterol from 220 to 190 milligrammes per 100 cubic centimetres of blood did take place, it was within the normal range of fluctuation. Later, the administration of 10 milligrammes of pure thyroxine dissolved in a little alkali was followed by a prompt rise in metabolic rate, from −21% to +3%. The rise in basal metabolic rate was directly proportional to the dose of thyroxine, namely, an increase in basal metabolic rate of approximately 2·5% to 3% per milligramme of thyroxine; a result similar to that obtained by Murray Lyon[15] following the administration of pure synthetic thyroxine to patients with typical myxœdema.

It is interesting to note that after the metabolic rate had been elevated by the thyroxine, it was maintained for several months above the normal level by the administration of only 0·36 gramme (six grains) of dried thyreoid substance *per diem*. This was probably due to a persistence of metabolic effect from the original 10 milligrammes of thyroxine (compare Thompson *et alii, loco citato*[15]).

Discussion.

Basal Metabolic Rate.

The two first patients, in whom a subnormal metabolic rate was associated with primary pituitary deficiency, responded to thyreotrophic hormone administration by a very definite elevation of basal metabolism. This rise attained its maximum one to two days after the last injection. The metabolism then fell, reaching the normal level in a week or ten days.

The patient whose thyreoid gland had been removed showed absolutely no change in metabolic activity after receiving the hormone. This corresponded to the results obtained by other workers, who have found that after experimental removal of the thyreoid from animals the calorigenic action of thyreotrophic hormone is absent.

Of the two subjects (Cases III and IV) with spontaneous hypothyreoidism, the one exhibited no increase in metabolic rate, the other only a slight elevation as a result of the administration of thyreotrophic hormone. This is in accordance with the results of most previous investigators, especially those of Scowen, showing that there is a lack of response to the hormone in myxœdema. One may presume that the thyreoid gland in the majority of these patients has so little responsive tissue left that it fails to react to stimulation by thyreotrophic hormone, sufficiently to elevate the basal metabolic rate.

Blood Cholesterol.

The relationship between the activity of the thyreoid gland and the level of blood cholesterol is well established. In myxœdema hypercholesteræmia is the rule, whereas in hyperthyreoidism the level of blood cholesterol is usually at the lower limit of normality or even subnormal. Treatment with thyreoid substance or thyroxine in adequate amounts is followed by a lowering of the blood cholesterol in myxœdema, concurrently with the rise of basal metabolic rate and improvement in the clinical condition.

The action of thyreotrophic hormone on the level of blood cholesterol has had scant attention in the literature, and then only in experiments on animals. Pugsley[9] (1935), injecting rats and dogs with a standardized thyreotrophic preparation, showed that the blood cholesterol level fell rapidly, reaching its minimum after about eight days and slowly returning to its former height in twelve to fourteen days.

Fenz and Zell[2][3] (1936 and 1937) describe experiments on a small series of rabbits in which

they found a fall in the cholesterol content of the blood within the first four hours of intravenous injection of "Hypothyrin", a thyreotrophic preparation.

In some experiments in this department we have found that in rabbits rendered hypercholesteræmic by prolonged cholesterol feeding a definite fall in blood cholesterol is observed after treatment with thyreotrophic hormone.

Normal fluctuations of blood cholesterol in man are quite considerable, but in any one individual, when blood samples are taken during fasting and analysed in a uniform manner, these should be at a minimum.

In Cases I and II (hypopituitarism) of the present series the rise in basal metabolic rate following the administration of thyreotrophic hormone was accompanied by a correspondingly pronounced fall in blood cholesterol, with a subsequent return to former levels.

In Case V (total thyreoidectomy) the change in blood cholesterol after administration of thyreotrophic hormone, although a fall, was so slight that it should probably be neglected.

In Case IV (myxœdema) the administration of thyreotrophic hormone was followed by a fall in blood cholesterol which seemed out of proportion to the slight elevation of basal metabolic rate; but it should be remarked that the number of control estimations was small.

This disparity between the changes in blood cholesterol and basal metabolism is exhibited in the most marked degree by Case III, that of the patient with hypothyreoidism, for here the blood cholesterol fell considerably (by about 100 cubic centimetres of blood), although the basal metabolic rate remained unaltered.

Although the fallacy of drawing definite conclusions from one or two cases is realized, certain possible explanations may be suggested. Firstly, the fall in the blood cholesterol level might have been effected by the stimulation of a residuum of thyreoid tissue which was not sufficiently large to elevate the basal metabolic rate. In other words, the cholesterol level of the blood might have responded more sensitively than the metabolic rate to a slight increase of thyreoid activity. Against this hypothesis, to some extent, are the findings of Schnitker, Raalte and Cutler (1936), that after total thyreoidectomy for heart disease had been performed on thirty-nine patients, the level of cholesterol in the blood rose in close correspondence with the fall in the basal metabolic rate. In favour of the suggestion is the negligible fall in blood cholesterol exhibited by the patient whose thyreoid gland had been removed. Secondly, the thyreotrophic hormone might have acted directly on the blood to lower the cholesterol level; or thirdly, the effect might have been produced indirectly through stimulation of some other endocrine gland, such as the adrenal. The question, however, must remain open until further investigations have been performed.

Symptoms.

Only one patient (Case II) exhibited any obvious clinical manifestations following the administration of thyreotrophic hormone, apart from a little local tenderness at the site of injection. This patient had swelling of the thyreoid gland, tremor, tachycardia and irritability.

She did, moreover, begin to menstruate again soon after the last injection and continued regularly for two more periods. This may have been the result of suggestion, rest in hospital *et cetera*; but probably is attributable to an improvement in ovarian activity following the general elevation of metabolism.

It should be stated that the preparation used contained quite negligible quantities of gonadotrophic hormone.

Therapeutic and Diagnostic Application.

In these experiments a standard dose of 4,000 units of thyreotrophic hormone, given in most cases on consecutive days, was employed to test the reactivity of the subject. No attempt has been made to prolong the treatment as a therapeutic measure, as up to now there are no indications for such use. Treatment with thyreoid extract in true myxœdema is very efficacious, whereas thyreotrophic hormone is valueless. In Graves's disease long-continued dosage with a view to development of antihormones is dangerous and has yielded negative results (Starr,[14] *loco citato*).

Those conditions which should provide the only fertile field for prolonged therapy with thyreotrophic hormone are those in which there is secondary hypothyreoidism due to a primary pituitary insufficiency. Some such patients respond to thyreoid extract less rapidly than do patients suffering from a similar degree of primary thyreoid insufficiency. Whether this lack of response is due to inadequate absorption of thyreoid hormone has not yet been settled (Lambie,[5] 1939).

It can be seen that a test dose of thyreotrophic hormone will help to distinguish between primary thyreoid insufficiency and hypothyreoidism secondary to pituitary insufficiency.

Summary.

1. Five patients suffering from different types of thyreoid insufficiency have received injections of thyreotrophic hormone.

2. Two patients with secondary thyreoid insufficiency showed elevation of basal metabolic rate following administration of hormone, two with primary hypothyreoidism responded very slightly, and a patient whose thyreoid gland had been removed gave no response at all.

3. In four of the five patients the administration of hormone was followed by a significant fall in blood cholesterol.

4. The relationship between the basal metabolic rate and level of blood cholesterol following administration of thyreotrophic hormone is discussed.

5. The therapeutic and diagnostic uses of thyreotrophic hormone are briefly discussed.

Acknowledgements.

I am grateful to Dr. W. C. B. Harvey, Dr. J. K. Maddox, Dr. J. H. Halliday, Dr. A. W. Morrow and Dr. N. R. Wyndham for permission to investigate their patients and publish the reports; and to the Board of the Royal Prince Alfred Hospital for these clinical studies. I wish to thank Miss Lesbia Wright, B.Sc., for the cholesterol estimations, and Mr. W. S. Stephen for technical assistance with the basal metabolic tests. I am indebted to Dr. V. M. Trikojus for his advice and help. I wish to thank Professor C. G. Lambie, in whose department this investigation has been performed, for assistance in the preparation of this paper.

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SULPHONAMIDE CHEMOTHERAPY IN GONORRHŒA.

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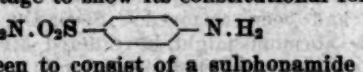
SINCE 1935, when Domagk published his important contribution to the study of chemotherapy, a considerable body of literature has been devoted to the therapeutic application of sulphonamide preparations in various types of infection. Their successful use in meningococcal infections was naturally followed by their application in gonorrhœa. Results generally were most spectacular. Nevertheless, the application of this new line of treatment is neither easy nor free from risk.

It requires emphasis that the body still needs to marshal the immune forces without which no infection can be cured. A full appreciation of this fact will help those who have to administer these new preparations to an understanding of the principles of administration and of the disadvantages attendant on improper use. Undoubtedly the administration of the sulphonamide compounds causes an arrest of bacterial growth. If the use of these preparations coincides with the period of maximum immunity response, it may result in the cure of the infection. On the other hand, if their employment is commenced before the immunity response has reached its maximum, it may result in an arrest of the immune response without cure of the infection. In these circumstances a relapse of the infective process usually occurs. It has too the further disadvantage that the natural immunity of the patient never becomes fully developed, and subsequent treatment with sulphonamide compounds is consequently less effective and may be harmful. Moreover, as with vaccine therapy, the most satisfactory results are obtained in the treatment of those who have a natural tendency to cure themselves, and the least satisfactory results are seen in those whose natural immunity response is conspicuously below normal.

Proprietary Nomenclature.

The chemotherapeutic experiments which initiated this new line of attack on bacterial diseases were commenced in Germany, and are closely associated with the name of Professor Domagk, who directed the experiments on animals at the laboratories of Bayer Pharma. A sulphonamide-containing azo compound, which showed some effect on streptococcal infection in mice, was the starting point for a number of other effective compounds. Of these, three were introduced commercially under the names of "Prontosil rubrum" (4-sulphonamide-2, 4 diamino-azo-benzol), "Prontosil soluble" (the disodium salt of 4'-sulphonamide-phenyl-azo-7-acetyl-amino-1-oxynaphthalein-3:6-disulphonic acid) and "Prontosil album" (p-amino-benzene-sulphonamide). As the last mentioned has come into general use and as some confusion has resulted from the variety of proprietary nomenclatures now in vogue, it may be an advantage to show its constitutional formula.



It will be seen to consist of a sulphonamide group (NH_2SO_2), a benzene ring, and an amino group ($N.H_2$). This compound is p-amino benzene sulphonamide; but as amino-benzene is aniline, it may be expressed also as aniline sulphonamide or more simply as sulphanilamide, which is the name now in

common use. This drug is now manufactured under a variety of proprietary names, in addition to sulphanilamide, such as "Streptocide", "Prontosil album" and "Sulphonamide-P".

Recently other derivatives have been placed on the market. Of these there may be mentioned two introduced by Messrs. May and Baker, "Proseptasine" (para-benzyl-amino-benzene-sulphonamide) and "T 693" (para-amino-benzene-sulphamido-pyridine) and another preparation introduced by Bayer Pharma called "Uleron" (amino-benzol-sulphonamide-benzol-sulphon-dimethylamide).

Method of Use.

The preparations referred to are chiefly employed in the form of tablets for oral use, usually of seven and a half grains or 0·5 gramme. Their action depends on a specific chemotherapeutic effect demonstrable only in connexion with the living body or its cells. One of the most outstanding observations, as pointed out by Felke,[1] is that they have no value as prophylactics. This at once suggests that they are effective only in the presence of an immune response on the part of the body and points the way to their effective clinical use. A "readiness to be cured" on the part of the sick body is an essential prerequisite for rapid cure. In acute gonorrhœa, during the first ten days or so, the disease is extending through the anterior part of the urethra. In the third week the posterior part of the urethra commonly becomes involved. On account of its rich vascular and lymphatic supply this at once results in a greatly increased immune response, as can be readily shown by the complement fixation test. Accordingly, these preparations should never be employed until this stage has been reached.

The dosage recommended by us is one gramme three times a day for four days. On account of the risk of toxic effects, the drug should be discontinued for eight days and then resumed for a further eight days. If an improvement is not secured at the end of this period it is useless to pursue this line of treatment.

Clinical Results.

Generally the result of treatment with sulphonamide drugs is very favourable. It may be said that in patients who respond to these drugs the improvement is often striking. Patients with a commencing posterior urethritis without involvement of the prostate gland or seminal vesicles usually improve rapidly.

In general, the complications of gonorrhœa are favourably influenced.

There is, however, an appreciable minority of patients in whom these drugs produce no improvement whatever and a smaller minority who become particularly resistant to treatment. In this latter class are fequently included those patients in whom the drug has been used before the immune forces of the body are fully developed. It should be emphasized that the sulphonamide preparations are not a substitute for the conventional methods of treatment and that local applications to the urethra, dilatation, investigation of prostate gland and seminal vesicles, and urethroscopy have their place as heretofore. Indeed, on account of the illusory appearance of cure achieved in many cases, they become more necessary than ever. It needs no stressing that a superficial appearance of cure is a potential danger for it encourages the patient to assume that he is cured without undergoing a routine examination of the urethral tract. Closed foci, infiltrations of the ejaculatory duct, sclerosed seminal vesicles and the like, yield only to appropriate local treatment.

Toxic Effects.

The various sulphonamide preparations vary in their toxicity. Sulphanilamide produces a bewildering array of toxic effects. As with other drugs susceptibility is the important factor. Nearly all patients suffer some toxic effect. In the majority it is of a mild character. Headache, giddiness, a sensation sometimes described as "punch-drunk", weakness and inability to concentrate are commonly encountered. Nausea, mild fever and fleeting skin eruptions are equally common. These effects need not usually interrupt the administration of the drug on the lines recommended.

More serious effects noted by us are diarrhœa and vomiting, high fever with or without morbilliform or scarlatiniform rashes, toxic nephritis, mental confusion, loss of memory and polyneuritis. In these circumstances discontinuation of the drug is indicated.

The more serious effects such as agranulocytosis, hæmolytic anæmia and toxic jaundice have not occurred in our experience of these drugs. In addition to discontinuation of the drug, they require therapeutic measures.

"Uleron" is among the least toxic of the various preparations and is usually well tolerated. Neuritic disturbances may supervene if the drug is administered over too long a period. The peroneal and tibial nerves are chiefly affected, a more or less marked stiffness of the leg muscles being caused. We have seen only one case of polyneuritis during our experience with this drug. It occurred in a patient with an alcoholic history. The appropriate treatment is injections of a vitamin *B* preparation.

A point to which some emphasis should be given is that patients to whom these various preparations are being administered should be seen daily.

Sulphur in any form should not be concomitantly taken. For this reason, eggs and onions, which contain a good deal of organic sulphur, should be forbidden as well as sulphate aperients and analgesic and hypnotic drugs derived from aniline, phenylhydrazinc and sulphonal. Where a laxative is required liquid paraffin is safe and effective.

The Standard of Cure.

It is perhaps necessary to call attention to the necessity of viewing this new method of treatment in its proper perspective. The greatest danger lies in the illusory appearance of cure achieved in many cases. The most satisfactory results are always

got in those with a high degree of natural bodily immunity. Improper use of the sulphonamide drugs results in a suppression of immunity. Thus some patients are made worse than they would otherwise be, while others become a potential danger to the community. The proper attitude, we believe, is to use these various preparations as a supplement to conventional methods.

Urethral irrigation and injection, dilatation of the urethra, the appropriate treatment of infected prostate gland and seminal vesicles, urethroscopy, and the examination of the blood by the gonococcus complement fixation test are still the essential procedures. The last mentioned examination in particular should never be omitted.

Subject to the foregoing remarks, we may conclude that sulphonamide therapy wisely employed lessens the duration of treatment in favourable cases.

Reference.

(1) H. Folke: *"Wie soll sich der Arzt in der Praxis zur Chemotherapie der Gonorrhoe stellen?"* *Münchener medizinische Wochenschrift*, Volume LXXXIV, November 19, 1937, page 1867.

FURTHER OBSERVATIONS ON ENDEMIC TYPHUS IN NEW GUINEA.

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In a recent article[1] one of us (C.G.) stated that discussion of certain aspects of the epidemiology of endemic typhus in New Guinea had to be postponed because until then no cases had been reported from the Aitape-Sepik district. A call to Wewak for a consultation on two patients was therefore doubly welcome. That an opportunity to collect information about some possible previous cases arose on the trip was a further fortunate happening.

Reports of Cases.

One patient, H.D.E., was infected probably at Green River Aerodrome, about fourteen miles from the border of Dutch New Guinea, and about eighty miles from the coast. The other, G.J.W., was infected in the Maprik gold-field area, about twenty-five miles in from Matapu. Their clinical histories are as follows:

Case I.—H.D.E., a male, aged thirty-eight years, a surveyor, left Green River Aerodrome on September 9, 1938, for Yagrona, feeling perfectly well. He became ill first on September 21, 1938, having a rise in temperature (which persisted in spite of quinine), headache and general malaise. A faint macular rash appeared on September 25, 1938. He was brought into Wewak by aeroplane and admitted to hospital on October 4, 1938.

On admission he was very weak. His temperature was 39·5° C. (103° F.), his pulse rate was 120 per minute, and his respirations numbered 32 per minute. He was cyanosed and slightly delirious. He had an eschar on the right leg just above the ankle. His mental condition became normal and his general condition improved until October 9, 1938. On that day he became weaker and his pulse became weak. He was given "Cardiazol" regularly after this. On October 10, 1938, he became restless, and the amount of sedatives given was increased. On October 12, 1938, he became semi-conscious, with Cheyne-Stokes breathing, and had every appearance of uræmic coma. The coma increased progressively, and he died on October 13, 1938, the twenty-third day of illness. His temperature remained in the vicinity of 39·5° C. (103° F.) throughout.

Case II.—G.J.W., a male, aged twenty-six years, was a recruiter. He had been in the Maprik area, within two days' walk of Maprik, from September 3, 1938, until October 1, 1938. He complained of feeling ill on September 30, 1938, with fever, headache and general malaise. On admission to hospital on October 5, 1938, his temperature was 39·8° C. (103·6° F.). His pulse rate was 100 per minute, and his respirations numbered 22 per minute. He complained of headache and generalized pains. He had a small sore on the dorsum of the penis just behind the corona. There was a faint red macular rash on the upper part of the abdomen and on the chest. General examination revealed no further abnormality. On the morning of October 6, 1938, several small urticarial patches appeared on the buttocks. By noon the trunk, arms and legs were covered with giant urticaria, which responded rapidly to treatment. On the evening of October 8, 1938, he had an acute attack of asthma, which was relieved by hypodermic injections of adrenaline. He had several further attacks of asthma at intervals during the next week. He gradually became more restless, toxæmic and cyanosed. He was transported by aeroplane to Wau (a distance of about 350 miles), where, on the sixteenth day of his illness, he was given a transfusion of approximately one pint of blood obtained from the last patient treated in Wau. He was very toxæmic, and the blood was given empirically, no time being taken to test its titre. He made an exceptionally slow recovery.

Discussion.

Serum Reactions.

At Wewak we performed hasty agglutination tests with improvised equipment, and found that serum from the first patient (H.D.E.), on the twenty-third day of the disease, agglutinated *Bacillus proteus* Kingsbury at a titre of approximately 1 in 1,280. From the second patient (G.J.W.) serum taken on the fourteenth day agglutinated this organism at a titre of approximately 1 in 80. The emulsion used was prepared in the laboratory of Rapindik Hospital, Rabaul.

TABLE I.
Agglutination Tests with Serum from Two Patients with Endemic Typhus.

Patient.	Day of Illness.	Organism.	Titre.										Control Titre.
			20	40	80	160	320	640	1,280	2,560	5,120	10,240	
H.D.E. ..	Twenty-third ..	*OXK*[1]	+	+	+	+	+	+	+	+	tr.	–	–
		X19[2]	–	–	–	–	–	–					–
		W[3]	–	–	–	–	–	–					–
G.J.W. ..	Fourteenth ..	*OXK*	++	+	+	?	–	–					–
		X19	–	–	–	–	–						–
		W	–	–	–	–	–						–

[1] *OXK* = *Bacillus proteus* Kingsbury, *O* form. [2] *X19* = *Bacillus proteus* Lister *X19*. [3] *W* = *Bacillus proteus* Warsaw.

The same samples when tested later at Bulolo under standard conditions gave the results shown in Table I.

The emulsions used were the following: *OXK*, prepared in the Bulolo Gold Dredging Hospital laboratory from a culture obtained from the Commonwealth Serum Laboratories; *X19* and *W*, standard emulsions obtained directly from the Commonwealth Serum Laboratories.

These tests, together with the clinical pictures, definitely classify these cases as identical with the various cases of endemic typhus already reported.[2][3][4][5]

On October 20, 1938, the twenty-first day of the disease and the fifth day after the blood transfusion, the second patient's serum had a titre of 1 in 1,280.

Other Possible Cases.

At Wewak we found brief references to three cases of "bush typhus" (*sic*) which had occurred during 1937. We were able to obtain fairly good details of his own case from one of these patients and a description of another. Whether these descriptions were accurate or not we cannot say; but they were quite positive, and we are both of the opinion that, considering the available evidence, these two cases did not correspond clinically with the type of endemic typhus under present observation. The third patient became ill at Yamil, about fifteen miles from Maprik, and was admitted to Wewak Hospital in August, 1937. He presented a typical clinical picture of endemic typhus.

To Mr. F. Cattell, senior medical assistant at Wewak, we are indebted for information about two probable cases that he has encountered. The first occurred on Karkar Island, near Madang, in 1937. The illness was provisionally diagnosed as cerebral malaria, but the symptoms did not respond to the administration of quinine. There was a continuous elevation of temperature until the tenth day, when the patient died. A rash appeared on the chest towards the end. The other case, which also occurred in 1937, was that of a young man who was engaged in clearing bush at Gunob. He had complained of severe itching of the legs at previous times. He had a continuous elevation of temperature for eight or nine days and then died. He did not respond to treatment by quinine, and there was no rash.

There is no positive evidence either for or against the presence of an eschar in these cases; but from what he remembers of them, Mr. Cattell believes that they resembled closely the two present cases. We are of the opinion, after considering the available evidence, that these were probably cases of endemic typhus.

In 1936 there was another definite case, the patient being a medical assistant stationed at Aitape. He contracted the disease in the mountainous country behind Aitape. The history was typical; there were a continuous elevation of temperature, not relieved by quinine, an eschar on the leg, a reddish macular rash, extreme prostration and vivid nightmares.

From a lay source general details of six cases that had occurred on the Siling River during the 1937 gold rush were obtained. As far as can be ascertained, they were all of endemic typhus.

Larval Mites.

The whole of the Sepik district is heavily infested with *bush-mokka*. Many islands off the coast are particularly bad; locally some are called "*mokka*-islands", and natives working on these have to stop frequently and wash with sea water to relieve the irritation.

One of us (A.G.S.) has recently visited both the Green River and Maprik areas. At Green River bush rats, of a species not yet determined, are to be found in enormous numbers. In the vicinity of Maprik bush rats and bush fowl are also plentiful.

So far only one species of larval mite has been obtained from the district: a species of *Schöngastia*, of which fifteen specimens were taken from two men

near the Suein River. Two specimens were also reported[1] from a bush fowl at Bulolo. Since then, six specimens have been taken from another bush fowl, and six from a man, both at Bulolo. These findings open up the possibility that this species is a vector of the disease; but until a proper survey of the mites and their hosts from the Sepik district can be made, and particularly until this species has been found on a rodent host, it must remain at best a probability.

Summary of Cases.

Cases have occurred in almost every part of the territory. In the list given in Table II one occurred in New Britain in 1930, one at Bulolo in 1932, and the others have all been reported since August, 1934.

Table II.

Distribution of Cases of Endemic Typhus in New Guinea.

District.	Area.	Number of Cases.	Number of Deaths.
Morobe	Wau	28	5
	Upper Watut	5	0
	Bulolo-Bulwa	4	0
	Ramu	1	1
New Britain	Kokopo-Bita Paka	2	1
Madang	Madang	1	1
	Karkar Island	(1 probable case)	(1)
		(1 probable case)	(1)
Sepik	Green River	1	1
	Maprik	2	0
	Altape	1	0
	Wewak	1	0
	Schilling River	(2 possible cases)	(0)
		(6 possible cases)	(0)

If the doubtful cases are omitted, it will be seen that of a total of 46, nine patients died—a mortality rate of 20%.

Of the three women included, two were pregnant, and both aborted. Of the patients who recovered, most were in hospital for one month.

Of the 28 cases from the Wau area, which comprise the only group large enough to bear analysis, the monthly distribution during four years is shown in Table III:

Table III.

Monthly Distribution of Cases from the Wau Area over a Period of Four Years.

Month.	Number of Cases.
January	2
February	1
March	2
April	1
May	0
June	1
July	3
August	5
September	2
October	6
November	2
December	3

That 21 or 75% occurred during the six months from July to December may be of significance for the Wau area; but since climatic conditions vary so widely in areas even closely adjoining, these figures can hardly be of value for the territory generally.

In the same group, the annual incidence since 1934 has been six, nine, five, five, three. Nothing of any value is to be gained from these figures.

There are still no records of cases occurring among natives, although a keen look-out has been kept.

Convalescent Serum.

McKenna, of Wau, has been using convalescent blood or serum empirically for some time in the treatment of severely ill patients, but no controlled observations of results have yet been made, and the data available are not enough to permit any conclusions to be drawn. There is good reason to suppose, however, that serum from a recent case may be of value in treatment.

Protective Measures.

From our present knowledge the following few protective measures can be suggested; they aim at minimizing the chance of contraction of the disease: (i) systematic trapping and burning of rodents around camp sites; (ii) restriction whenever possible of activity by white people to pathways and clearings that have been burnt off; (iii) bathing immediately on coming in from work, particular attention being paid to the selected sites; (iv) observation of the selected sites for the earliest appearance of the eschar; (v) excision of the eschar widely, before the onset of general symptoms.

We suggest that all field workers should be supplied with a set of instructions embodying these points, with sufficient explanation to make them intelligible to laymen. The circular that has been adopted by Bulolo Gold Dredging, Limited, Oil Search, Limited, New Guinea Goldfields, Limited, and Guinea Airways, Limited, for general distribution appears in the appendix. It is, of course, obvious that the stating of certain speculative points as if they were established facts is essential if a circular of this nature is to be of any value at all.

Acknowledgements.

We are indebted to Dr. N. McKenna, of Wau, for details of the second case after he took over care of the patient, and for much helpful discussion on many points. Mr. O. B. Hart, manager of Bulolo Gold Dredging, Limited, has shown his active interest by authorizing the production and distribution of circulars to all who are interested, with the company's compliments.

Appendix.

Endemic Typhus ("Japanese River Fever").

1. This is an important disease, since it involves a month's illness and requires skilled nursing. Men working in the bush, especially in newly cleared areas, are particularly liable to contract it, but there is every chance of avoiding it if the instructions outlined below are followed.

2. The disease is conveyed to man by the bite of an infected *bush-mokka*, which gets its infection from a

bandicoot or a rat. *Mokkas* are particularly numerous along river valleys, and in *sak-sak* and *pit-pit* swamps. They usually get onto man as he brushes against vegetation, or when he sits on the ground, or on logs or stumps.

3. The *mokka* usually selects certain sites to bite—the armpits, waistline, groins, penis, scrotum, legs and ankles. A bath should be taken immediately on coming in from work, and these sites should be scrubbed with a coarse sponge or a soft nailbrush, with a thick lather of soap, in order to remove as soon as possible any *mokkas* which may be there.

4. When possible, paths should be made at least three feet wide; the grass and brush should be burnt where it lies, together with that bordering the path. All whites should try to keep on such paths, or to remain in small clearings prepared in a similar manner, while working or supervising natives at work. Natives may safely carry out the work of clearing, since they do not suffer from the disease.

5. Natives should be encouraged to trap and burn bandicoots and rats around camps which are likely to remain for any length of time. *Kau-kau* or *tapiok* should be used to bait traps, or oil of aniseed may be used as a lure. Traps are best set overnight. Refuse likely to attract rats should be properly disposed of.

6. Whereas an ordinary *mokka* bite itches severely, an infected one does not, and so is likely to be missed unless the selected sites are inspected regularly. An infected bite appears as a dark red or purple area (one-quarter to one-half inch across) surrounded by a dull red ring (about one-eighth to one-quarter inch wide). Later the central part becomes a tough black scab, dry, and firmly attached. It is usually free from pain, tenderness and itching.

7. Such a sore should be shown to a doctor as soon as it is noticed, as there is a chance that if it is cut out in time the threatened attack may be avoided.

8. Should an attack develop, it will almost certainly be mistaken for malaria in the early stages; but persistent high temperature in spite of taking quinine, and the presence of the typical sore should correct the diagnosis. The patient should be got into hospital at once before he becomes "light-headed".

9. Great assistance in the study of this disease can be given by collecting *bush-mokkas*. They are red, orange, or yellow, about one-half the size of a pin's head. They can be dug out of the skin with a needle. They can also be found singly or in groups, on the head, neck and legs of ground-birds, on the ears, nose and abdomen of rats, and on the ears, nose, pouch or scrotum of bandicoots. Patches of skin from game should be cut out, or better still, the heads of birds or whole rats may be collected. They should be preserved in spirit.

References.

(1) C. E. M. Gunther: "The Probable Vector of Endemic Typhus in New Guinea", THE MEDICAL JOURNAL OF AUSTRALIA, August 6, 1938, page 202.

(2) B. A. Sinclair: "A Possible Case of Japanese River Fever Occurring in the Mandated Territory of New Guinea", THE MEDICAL JOURNAL OF AUSTRALIA, December 6, 1930, page 759.

(3) C. E. M. Gunther: "Endemic Typhus in New Guinea", THE MEDICAL JOURNAL OF AUSTRALIA, June 29, 1935, page 813.

(4) R. H. von der Borch: "Non-Epidemic Typhus: A Report on Fourteen Cases Occurring on the Goldfields, Wau, Mandated Territory of New Guinea", THE MEDICAL JOURNAL OF AUSTRALIA, March 20, 1937, page 435.

(5) C. E. M. Gunther: "The Serology of Sixteen Cases of Endemic Typhus in New Guinea", THE MEDICAL JOURNAL OF AUSTRALIA, March 20, 1937, page 439.

COMPARATIVE ANATOMY OF THE KNEE JOINT IN RELATION TO CONGENITAL ANOMALIES.[1]

By STUART SCOUGALL,
Sydney.

AN understanding of the evolutionary factors governing our present anatomy is essential to a full understanding of congenital anomalies, their ætiology, pathology and treatment. Fortunately this evolutionary history is often available to us, and sometimes in detail, in a study of the phylogenesis of the race, and this history is, in unseen pageantry, briefly reenacted in the embryological development of the individual. The embryo has not the direct power of forming new structures specifically for adaptation to a change in environment; but it has the power of recapitulating the centuries of slow evolution of its ancestors and of cutting down the period to a few days. Some new structure, then, at this stage may be evolved, lengthening the chain; but the inner processes of this aparently blind natural selection are not yet fully understood.

As an example, the primitive backbone or notochord is soon replaced by cartilage, which in its turn is replaced by bone, and this embryological sequence has its parallel in phylogeny. Man in his ontogenetic development passes rapidly along the phylogenetic route and furnishes a condensation of his genealogical history, the slow motion of which over those incredibly long æons of time would stir envy in the modern producer in its dramatic power.

A brief review of our locomotive progress is of interest. As water was originally the exclusive medium of animal life, the change to the amphibian type became inevitable with the gradual appearance of swamps and finally of dry land. The South American dipnoan (*Lepidosiren*) is generally accepted as the starting point in the evolution of the fin into a limb, though alternative suggestions have recently been made by both Kerr and Gregory.

Kesteven was the first comparative anatomist to point out the great significance of the segmental arrangement of the muscles in the fin of the Queensland lung fish (the archipterygium of *Neoceratodus*). It appeared to him that an essential stage in the evolution of the fish fin (moved as a whole by single adductor and abductor muscles) into the jointed tetrapod limb was some primitive segmentation of the two groups of muscles. This primitive segmentation is certainly present in the fin of our lung fish. We find here, beyond the powerful abductor and adductor muscles, a whole series of short abductor and adductor muscles along the numerous skeletal segments at the termination of the limb. Kesteven has also shown these lung fish to be very primitive amphibians, so that a strong case is made for evolution from the fish fin, and the dipnoan is the most primitive limb known.

The subsequent changes in the topography of the earth's surface, its vegetation, climate and other factors, have necessitated the subsequent modifications and adaptations up to our present architecture in function.

Herzmark has just given us a survey of the evolution of the knee joint, with dissections at stages throughout the long trail.

It will be seen that complete extension of the knee joint occurs only in man, though the position is almost achieved in the elephant. In man this position of extension is accompanied by the passive

[1] Read at the annual meeting of the Australian Orthopædic Association in March, 1938.

locking mechanism. It is interesting to note in passing that the corresponding joint in the horse, called the stifle joint, remains in a condition of moderate flexion, there being no passive locking mechanism. It is of further interest to note that the horse, though he occasionally sleeps lying down, habitually does his sleeping in the standing position. So far as the anatomical construction of the knee is concerned, it should be easier for us to sleep on our feet; but the possession of this horse sense is obviously lacking in man. To what extent this accomplishment does exist in man is a controversial question.

There has been little change in the knee joint of man from the primitive forms, in comparison with the great changes that have taken place in the remainder of the body.

The limb buds arise in the human embryo at four weeks, and by seven weeks cartilage centres appear for the bones of the lower extremity. The reptilian stage is reached by eight weeks, the fore limbs being internally rotated, while the hind limb is in external rotation and the knee is at a right angle.

The fibula becomes excluded from the knee joint at eight weeks.

The joint space is present by nine weeks, and the synovial membrane and capsule are both formed by the perichondrium.

In one branch of the Reptilia the meniscus is represented by a continuous sheet or disk. This persistence occurs as a rare anomaly in the human knee joint, and has to be borne in mind when bilateral symptoms, often associated with creaking, appear at about adolescence. Such a patient has been seen at the Royal North Shore Hospital, and the history is recorded here for its interest.

A young woman, aged twenty years, was first seen in the out-patient department, Royal North Shore Hospital, on May 12, 1936, complaining of disability in both knees since the age of fifteen years; the right knee was more affected than the left. Discomfort came on insidiously, both knees being affected, one shortly after the other. There was no history of trauma. There was frequent, almost constant creaking and cracking, of four years' duration; this again was more pronounced on the right side.

For the last eight months pain and slight swelling had been present on the outer side of the right knee, and during the last three months the knee had begun to give way occasionally. The left knee had been cracking fairly constantly for eight months. There was only a trace of effusion and no comparative atrophy in the thighs. Creaking could be elicited throughout the lateral side of the knee joint, and a loud crack was present at about 15° of flexion from the extended position of the knee.

At operation the lateral meniscus was present in the form of a continuous disk, with the greatest thickening at the periphery, though no gross lesion was found in this disk.

In the condition of osteochondromatosis of the knee joint the origin of the cartilaginous nodules from the synovial villi can be readily understood, in view of the origin of the synovium from the perichondrium. At this stage there are five synovial cavities, one between the patella and femur, while the continuous disks create four more cavities between the condyles of the femur and those of the tibia. The increase in condylar area gives extra surface for weight bearing; but it is to be noted that osteoarthritis, with its relation to the trauma of weight bearing, occurs much more frequently and to a greater extent at the knee joint than at the ankle joint, with its smaller bearing surface.

The patella in general tends to increase in size and range of movement as compared with the earlier forms, and this progressive size and range suggests increasing function. Herzmark states that the thickness of the patella carries the patella tendon more anteriorly and thus increases the tension on the quadriceps; but tension must primarily be due to the quadriceps itself.

Maloney, in *The Journal of Bone and Joint Surgery* of July, 1937, after a review of the literature on the subject, discusses the mechanics of congenital absence of the patella. His conclusions are as follows:

1. The patella may be absent due to congenital or hereditary causes.
2. Congenital absence of the patella is associated with other isolated grotesque anomalies, and with marked impairment in function of the knee joint.
3. The hereditary absence of the patella is usually associated with but one remote anomaly, absence of the thumb nails; and there is no evident impairment in the function of the knee joint.
4. The patella is not a lever.
5. The femoral condyle is not an efficient inclined plane.
6. The patella owes its efficiency to increasing the distance between the axis of rotation of the tibia and the line of direction of the force which falls on the tibial tubercle, which means the patella ligament, thereby decreasing the magnitude of the force factor in the product (magnitude of force times the perpendicular distance between the centre of rotation and the line of direction in which force is exerting itself) that gives the moment of force sufficient to rotate the tibia.

Congenital dislocation of the knee joint may be accompanied by absence of the patella, which soon appears, however, after reduction of the dislocation, with resultant pressure on the *ligamentum patellæ* by the condyles of the femur. In the anthropoid firm pressure and close coaptation have in association a rudimentary patella.

Herzmark found the cruciates in the animals dissected relatively much larger than those found in man, reaching their greatest size in the cat and the macaque. Greater calls on the tension on the cruciates are made in those tree-climbing animals than in plantargrade man, who rarely places tension upon those ligaments—except, of course, the man on the flying trapeze. But even in such an acrobat those ligaments as at present existing in man stand up to tension in this manner.

Are we to deduce from their decreasing size a vestigial significance?

It would appear that greater calls on these structures were necessitated in the arboreal life of the monkey. It must be remembered also in this connexion that the cruciate ligaments became intra-articular as the condyles moved further back and included portion of the capsule.

The menisci reach their maximum development in man, and Herzmark states that since the menisci are fibro-cartilaginous they will redevelop if the synovial attachment is left intact. He suggests the leaving of a rim of the meniscus attached to the synovial membrane. After complete removal of the meniscus from man there is a wedge-shaped regeneration of firm, dense tissue which extends inward in imitation of the disk.

There is an idiopathic type of posture deformity at the knee joint, apart from those caused by such gross diseases as rickets. Included among such deformities are *genu valgum*, *genu varum* and *genu recurvatum*, which in the older conception were explained by mechanical causes, such as abnormal static conditions, faulty attitude, overweight *et cetera*. This idiopathic form is rarely of an extreme degree.

Max Böhm, in *The Journal of Bone and Joint Surgery* of July, 1932, has given us evidence of the occurrence of this idiopathic type very recently in the genealogical tree. In the anthropoid ape the lateral condyle of the tibia is always much broader and higher than the medial condyle, whereas in man these condyles are of the same height and in general concave.

As late as seven months the human fœtus has the anthropoid characteristics in the tibial epiphysis, high convex lateral condyle and low concave medial condyle. With the joint surfaces in position the shaft of the tibia is deviated inward, the result being a *genu varum*. These relations persist in young children, who have the same high convex lateral condyle and low concave medial condyle and deviation of the shaft, often the cause of anxious inquiry by the mother in the early weeks of the child's life. The long climb by the phylogenetic route does not cease at birth, nor would we expect it to do so, though it is scarcely noticed, even when the unfolding occurs under our own eyes. It takes twelve years for the epiphysis to become symmetrical—that is, for both tibial condyles to reach the same height and become concave, and for the shaft of the tibia to grow straight.

My second boy, who had a *genu valgum* with a three-inch gap at the age of three years, now has a mild *genu varum*, with a one-inch gap at the knee, at the age of twelve years, without treatment of any kind. This type of abnormality has to be kept in mind when the procedures to be adopted for postural disabilities at this joint are being evaluated. We see very little adult *genu valgum* or *genu varum*.

In the anthropoid the medial condyle of the lower end of the femur is higher and larger than the lateral condyle. This difference is reached just before adult age, as also are the changes in the tibia. But here in the femur the changing shape is not complete until maturity, when the condyles are of equal size, shape and height.

Böhm has shown these characteristics to exist in the femur in gradually decreasing degree throughout fœtal life and childhood into maturity. An arrest of development causes *genu valgum*.

The *genu recurvatum* is less common and is generally associated with *genu valgum* or *varum*. In the anthropoid the head of the tibia is curved backward. This *genu recurvatum* is seen in the human fœtus and does not finally disappear until the tenth year. In the anthropoid the curve of the condyle in the lateral view forms part of a circle; but in the human this is much flattened. These condyles are round in the human embryo; they persist in this shape after birth, and gradually change to the adult type.

Congenital *genu recurvatum* results from the persistence of the circular condyle and curved back condition of the tibia.

Böhm discusses the radiological appearance of these deformations: the epiphysis is asymmetrical while the shaft is flat.

In cases due to rickets the reverse condition holds: the shaft is deviated and the condyles are not abnormal. He states that with the continuance of arrest in development the erect posture and gait produce, increase and stabilize deformities.

In the modern adult European tibia the surface of the lateral condyle generally has a slight convexity from before backward. In savage races this convexity is very much greater. The slender character of the epiphyses of the tibia in the Australian aboriginal is very striking, especially in relation to the great length of the bone. The average transverse diameter of the proximal epiphysis is found to be 69 millimetres, which is much smaller than that recorded for any other races, with the exception of the few examples of very short tibiæ. The head of the tibia in the aboriginal is definitely retroverted; the average angle is 17° in a series of 240 cases. This retroversion is due to a backward curvature of the upper part of the shaft. The condyloid surface will be at an oblique plane backward and downward if the shaft is placed in a vertical position. This is found in some other primitive people and in Neanderthal man.

There is no evidence that this condition has resulted in any alteration of posture in the general alignment of the aboriginal limb. Osteoarthritic changes in the aboriginal are found almost exclusively at the proximal end of the tibia. The convexity of the outer condyle of the tibia diminishes slightly through the savage races, and is but slight in man. It is to be noted that the posterior border is especially rounded off in the external condyle to facilitate the wider range of movement of the condyle with its loose attachment.

The two bones (tibia and fibula) are never permanently crossed or capable of any considerable amount of rotation, as in the corresponding joints of the fore limb; but in the climbing Australian phalangers and koalas, which have broad hind feet with an opposable hallux, there is greater freedom of movement between these two bones than in any other mammal. This does approach in some degree the rotation permitted by the radius and ulna.

Congenital dislocation of the knee is of two types: that due to primary embryonic defect and that due to malposition in the uterus. When congenital dislocation occurs in association with other germ plasm defects it is due to the primary embryonic defect. Such deformities are not, in general, amenable to conservative treatment. The second type is not accompanied by serious defects, and as a rule responds to manipulation aided by subcutaneous tenotomy. The majority of cases belong to this second type.

Reports of Cases.

A FURTHER CASE OF HUMAN INFECTION WITH TRICHOSTRONGYLUS COLUBRIFORMIS IN NEW SOUTH WALES.

By G. A. M. HEYDON, M.B., D.P.H., D.T.M. & H.,

AND

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NEMATODE WORMS of the genus *Trichostrongylus* are parasites of mammals and are commonly found in domestic herbivora. Although individually slender and small (usually five to eight millimetres in length) they are sometimes present in many thousands and may then cause the death of young stock. In heavily infested lambs the most typical symptom is diarrhœa (black scour); concurrently with this the animals lose condition and become anæmic.

Cases of *Trichostrongylus* infection in man have been reported from many countries, and with several species of the genus. Most of the species, as in the cases first found by Looss in Egyptian fellaheen, are normally parasites of sheep and other domestic herbivora. In man the number of worms is usually not large, nor have pronounced symptoms been reported. One species, *Trichostrongylus orientalis*, is not uncommon in the rural population of parts of Japan, Korea, Formosa and central and south China, and has been found in Armenians;[1] it has also been found in fat-tailed sheep and Bactrian camels;[2] of the genus *Trichostrongylus* it is the only species first found in man. According to Faust,[3] man appears to be the common natural host, while other mammals are only incidentally infected.

These trichostrongyle infections in man are usually brought to light by discovery of the eggs in the fæces in the course of routine surveys; for instance, hookworm surveys. From the eggs alone the species of the genus concerned cannot be determined. Officers of the Australian Hookworm Campaign supposed that the eggs found might be those of *Trichostrongylus orientalis*, but could not recover adult worms to confirm this.

Heydon and Green[4] in 1931 fed young goats with larvæ cultured from the fæces of human subjects from a sheep property on the Atherton Tableland, and from the goat-infested town of Mareeba. Most of the adult worms so obtained were *Trichostrongylus colubriformis*, a common parasite of sheep and goats, although two other species were obtained, *Trichostrongylus extenuatus* (*Trichostrongylus axei*) and a species of an allied genus, *Hæmonchus contortus* (an important and common parasite of sheep).

From 1919 to 1928 the Hookworm Campaign staff examined over 300,000 specimens of fæces from all States of the Commonwealth;[5] but only in the years 1923 to 1928 are reports of *Trichostrongylus* infection to be found. Before this the infections either were not found or were not recognized and regarded as hookworm ova, which they resemble to some extent. In the latter period, when the campaign worked mainly in Queensland, sixty cases of *Trichostrongylus orientalis* were reported from that State; twenty-seven of these are mentioned by Heydon and Green.

The districts in which infections occurred were those in which sheep or goats, or both, were common; for instance, Mareeba had 13 cases in 1,186 examinations, and Cooktown five cases in 410 examinations. In the intensely cultivated sugar districts these animals are few, and only one case was reported. It is probable that most of the parasites were *Trichostrongylus colubriformis*, or at least were acquired from sheep or goats.

In 1937 Clunies Ross[6] reported two cases in his laboratory staff; both persons had been engaged in experimental work on sheep trichostrongyles. Larvæ from one of these patients were fed to a young lamb, which developed an infection with *Trichostrongylus colubriformis*.

In this paper another case is reported, the first from New South Wales, apart from those of Clunies Ross in laboratory workers. This was found while the fæces of children in the Royal Alexandra Hospital for Children, Sydney, were being examined for the incidence of intestinal parasites.

Clinical Record.

I.H., a female, aged four years, under treatment for burns, was found to be passing eggs resembling those of *Trichostrongylus* in shape, size and stage of development. The average measurements were 90μ by 47·5μ.

It has been shown[7] that rabbits may harbour *Trichostrongylus colubriformis*, although their commonest species is *Trichostrongylus retortæformis*. It was therefore decided to try to obtain the adults in laboratory rabbits, in view of the practical difficulties of using lambs or kids.

A fresh specimen was collected for culture, and about twenty-five of the larvæ so obtained were fed to a young rabbit bred at the School of Public Health and Tropical Medicine, Sydney. *Trichostrongylus* infection has never been found in these rabbits. Three other rabbits of a similar age, one of them from the same litter as the test animal, were used as controls. Twenty-five days later *Trichostrongylus* eggs were found; an examination at twenty days revealed none.

On the forty-seventh day after infection the test animal was killed and one male and four female trichostrongyle worms were recovered from the upper part of the small intestine. The control rabbits remained completely free from all intestinal worm parasites for a further seven weeks, when the examinations were discontinued.

Discussion.

The separation of the different species of the genus *Trichostrongylus* is more easy and certain from the characters of the males than from those of the females. A comparison of the spicules, bursal rays and other features of the male with the figures and descriptions of Looss and of Nagaty left no doubt that the species was *Trichostrongylus colubriformis*. The latter author has recently revised the genus;[8] his description of *Trichostrongylus colubriformis* is based on material that included type specimens from man, sheep and goat, originally described under the synonyms *Strongylus subtilis* Looss, 1895, *Strongylus instabilis* Railliet, 1893, and *Strongylus colubriformis* Giles, 1892.

The four female trichostrongyles oculd not be definitely assigned to any one of several species, although they agreed well with the measurements and descriptions of *Trichostrongylus colubriformis*. The upper and lower limits of the measurements given by Nagaty show considerable overlapping for different species, and it is not impossible that more than one species of female was present and that the infection of the child I.H. was a mixed one. *Trichostrongylus rugatus* has often been found in sheep in New South Wales,[9] and the females

are indistinguishable from *Trichostrongylus colubriformis*. The shape of the female tail is regarded by Nagaty as a point of differentiation between *Trichostrongylus capricola* and *Trichostrongylus colubriformis*; in this respect our specimens resembled the latter, and we do not know of the presence of *Trichostrongylus capricola* in Australia.

The family of which this child was a member had lived in Leura until about six months before the finding of eggs, after which they lived in a suburb of Sydney. While they were in Leura, goats had been kept; it was probably from these that the child acquired her infestation. Infestation is acquired by animals by the swallowing of third-stage larvæ, which crawl from the ground surface onto blades of grass and are resistant to desiccation. No treatment of this child was attempted.

Cases of human infestation with these sheep trichostrongyles probably occur throughout the sheep country of Australia, but escape notice from the absence of symptoms.

Summary.

1. A further case of human infestation with *Trichostrongylus colubriformis* is reported from New South Wales.

2. The species was determined by infection of a laboratory rabbit.

3. Thirty-three unpublished records of the occurrence of *Trichostrongylus* infection in man in Queensland are collected.

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Reviews.

REFRACTION OF THE EYE.

A SECOND edition of "Refraction of the Eye", by Charles Goulden, has been published.[1]

The book has been, ever since the first edition appeared in 1925, the recognised text-book from which post-graduate students have studied the subjects of optics and refraction in preparation for the English diploma in ophthalmic medicine and surgery.

As the author states in the preface, there are no fundamental changes in this new edition; and indeed this is so: the text and illustrations, except for a few exceptions, are a reprint of the first edition.

Thorough explanation is given of the physical and physiological optics so necessary for the thorough understanding of the practical refraction of the eye, such as the laws relating to reflexion, mirrors, lenses, refraction of light and prisms, together with the optical constants of the eye.

The errors of refraction, myopia, hypermetropia, astigmatism *et cetera* and their treatment are then thoroughly explained.

The author then goes on to discuss the theory and use of the ophthalmoscope and retinoscope, and in the last chapter explains the muscular anomalies — strabismus, heterophoria—including their treatment.

The book is a sound text-book, neither too involved nor too elementary, and can be confidently recommended to those who may wish to get some understanding of this branch of ophthalmology.

[1] "Refraction of the Eye, including Elementary Physiological Optics", by C. Goulden, O.B.E., M.D., F.R.C.S.; Second Edition; 1938. London: J. and A. Churchill. Demy 8vo, pp. 287, with illustrations. Price: 12s. 6d. net.

J. B. MURPHY.

IT is with mixed feelings that one completes the reading of "Surgeon Extraordinary". Admiration for the brilliant surgeon mingles with regret that so great a man should have shown so little judgement in dealing with his fellow medical men, so little discretion in publishing his views far and wide.[1]

Dr. Cronin in his preface has somewhat overstated his praise for the work of the author, Dr. Loyal Davis, in calling his style "miraculous" and his book "glorious". Discounting these over-laudatory statements, "Surgeon Extraordinary" is a book which is well worth reading, as it gives a vivid picture of a great surgeon and interesting glimpses of the medical practice of his time.

John Murphy's parents came from the poorest of Irish peasantry. The famine of 1846-1847 drove both families across the seas to the promised land of the United States of America. Michael Murphy did not meet his future wife, Anne Grimes, until they met as settlers in the wilderness of Wisconsin. John Murphy was born in December, 1857, and his boyhood years were spent in the drudgery of farm work. The Murphys, father and mother, especially the mother, believed firmly in the advantages of a good education. Murphy in after years often quoted his mother's creed: "If you are educated there are no man's achievements which you cannot equal or exceed, provided you have industry and integrity and are temperate."

First attending the little local school, Murphy passed on to the high school and then worked in the local druggist's store. One day he assisted the local physician, Dr. Reilly, with a case and a friendship sprang up which led to his serving as the doctor's assistant for a short period.

Murphy's family wished him to be a school teacher, but a few months' trial of the teaching profession convinced young Murphy that he was misplaced. Dr. Reilly once again came into the picture, and for the sum of two hundred dollars agreed to teach his apprentice the medical art. Dr. Reilly was evidently a man of progressive ideas and soon advised his pupil to study at Rush Medical College in Chicago. A few months' study at this college confirmed Murphy in his determination to specialize in surgery. Gaining the appointment as intern at the Cook County Hospital he never missed an opportunity of gaining surgical experience, and incidentally he gives us a good account of the early days of Listerism and the use of the carbolic spray. He next went into partnership with a Dr. Lee in Chicago, and after a year with him made his long-hoped-for trip to Europe. There he made lasting friendships in Germany and Austria with Billroth and Schröder.

Returning to America and Chicago in 1884, he was soon in full practice with Dr. Lee. In 1885 he married the daughter of one of his patients, and in his wife he gained his greatest admirer and one who helped him to gain his future successes. In 1886 riots took place, and by the explosion of a bomb over one hundred policemen were injured and Murphy had his first great opportunity to do surgery on a large scale. Called as a witness at the

[1] "Surgeon Extraordinary: The Life of J. B. Murphy", by L. Davis, M.D., M.S., Ph.D., with a foreword by A. J. Cronin; 1938. London: G. G. Harrap and Company Limited; Australia: Angus and Robertson Limited. Demy 8vo, pp. 287. Price: 8s. 6d. net.

ensuing trial, Murphy gave his evidence dramatically, and being fully reported in the local Press, immediately became a local celebrity. The other doctors resented this publicity and accused Murphy of advertising. Thus was born the reputation that he always sought the limelight—a reputation which followed him to his grave.

The next few years were full of work—surgery by day and the evenings occupied with experimental surgery on dogs, in which his wife was his devoted assistant. In March, 1889, Murphy performed his first appendicectomy. He read a paper before the Chicago Medical Society, which received his teaching as to the necessity of the operation with ill-concealed ridicule and disapproval. He fought on and when he next faced the society he had two thousand cases to support his arguments. In Murphy's own words: "Looking backward, one can scarcely comprehend how a so-called intelligent profession was so slow in accepting the overwhelming force of numbers and facts, which could not be altered by theory or speculation. . . . Everyone recalls how reluctantly the advocate of the soothing lullaby of the opium treatment vacated his position, and how equally persistent and belligerent was the advocate of the death-groaning calomel and castor-oil participant."

Overwork at last called a halt, and tuberculous disease, which had proved fatal to several members of his family, seemed about to claim another victim. Eight months at Colorado Springs restored him to health, and then an invitation to the chair of surgery at the Rush and Chicago Medical College brought him back to Chicago. During his vacation Murphy had thought out the theory of his button, and after experimenting on a dog used it for the first time on a patient at the Cook County Hospital. As usual, his new discovery met with much opposition, and the papers getting hold of the controversy, once again Murphy was front-page news and anathema to his fellow practitioners; and among his bitterest opponents was the famous surgeon Nicholas Senn, who was President of the American Medical Association.

An invitation to address the eleventh annual International Medical Congress in Rome was accepted, and his tour of Europe, which followed the congress, was a triumph. The greatest surgeons—von Bergmann, Kocher, MacCormac, Macewan—greeted him with open arms.

On his return Murphy found his opponents, led by Senn, in full fighting array. In his clinic his surgical nurse would hand Senn a sterilized Murphy's button for use, and each time Senn would throw it dramatically onto the floor before proceeding with his operation.

In a review it is impossible to tell in detail Murphy's innumerable additions to surgical science. The surgery of the Gasserian ganglion, end-to-end anastomosis of blood vessels, surgery of the kidneys and prostate, collapse of the lung in tuberculous cavities, all intrigued his restless spirit, and he worked far into the nights seeking new methods.

Troubles and honours gathered around Murphy as the years passed. In his early married years he had to watch his only son die slowly of suffocation caused by the then almost universally fatal diphtheria. The first symptoms of coronary disease, which was ultimately to claim him as a victim, made its appearance. A controversy raged in the newspapers over the evergreen question of fee-splitting, and once again Murphy rushed into print in condemnation of this practice, and was accused by his colleagues of again seeking publicity. Elected in spite of all President of the American Medical Association, Murphy gave one of his best orations, full of wisdom and sage advice. His explanation of the success of the quack practitioner might be read with advantage by the members of the councils of our own Branches of the British Medical Association. His demand that the medical profession start a campaign of education of the public on medical subjects might well be acted upon here in Australia. Here are his words: "By advertisement they [the quacks] educate the people in their theories, beliefs or sophistries; and that is what the public wants—in fact what it demands. What has the regular profession done to educate the public in the last two centuries? Nothing! We have demanded of the public our acceptance on blind faith, and the age of blind faith in individuals is passed." Words true in the United States in 1911 and no less true in Australia in 1939.

An attempt to assassinate President Theodore Roosevelt was made and the President received a superficial chest bullet wound. The story of events from a medical point of view makes strange reading, and once again Murphy handled, not the patient, but his colleagues in the case, to say the least, tactlessly, and laid himself open to grave criticism.

In 1913, Murphy, in company with Cushing, William Mayo and Crile, was made an honorary Fellow of the Royal College of Surgeons of England.

Incessant work at last claimed its victim and a rest became imperative; but it was too late, and on August 11, 1916, as he crossed his room to greet his wife, he collapsed at her feet and died.

It is difficult to judge John B. Murphy. One is torn between admiration for a very great surgeon and regret for the failings of the man. It has been said that all men have their cross to bear. Truly Murphy had a very heavy one. He all his life sought for the approval and friendship of his fellow medical men, and yet his greatest discoveries only added to the number of his enemies. As his biographer says: "There was good and bad in this man—and in abundance on both sides." May we not say of him in reversing the old saying: "The bad was buried with his bones, the good has lived on in his gifts for the advancement of the surgical art."

A HAND-BOOK ON CARDIO-VASCULAR DISEASE.

"THE General Practice Series" has been increased by a decided acquisition in Terence East's "Cardiovascular Disease in General Practice".[1] To the cardiologist this book bristles with statements to which exception might be taken on the grounds that they are too sweeping or that they omit many controversial points. However, we must remember that it is written for the general practitioner who has not the time to concern himself with the fine points which are mainly of academic interest. His need is to know what happens in the majority of cases. This book fills the bill most adequately in that a somewhat dogmatic style makes it easy for the reader to grasp and to retain the facts presented to him. It is rather a pity, however, that such a useful volume should jar the reader with so many misprints.

Perhaps the most important feature is the space devoted to heart failure, the presence or absence of which is recognized by cardiologists as being the most important feature in any clinical case. Those who have the teaching of students among their activities would do well to read this book, paying special attention to the above section; although it does not contain all they require, yet it presents in clear relief the majority of the essential points.

The chapter on peripheral failure calls attention to a feature which is now beginning to receive more of the attention that it merits.

The author does the general practitioner a great service when he devotes space to such problems as the cardiovascular system in anæmia, minor infections, anæsthesia, pregnancy and athletics. Here he explodes some of the ancient but evergreen myths, and points out the way in which the damage may be assessed and the later effects visualized.

Problems of insurance and the diagnosis of the normal heart are other points on which the author gives some useful assistance.

We can thoroughly recommend this volume to the general practitioner as a clear exposition of those problems which he meets from day to day.

[1] "General Practice Series. Cardiovascular Disease in General Practice", by T. East, M.A., D.M., F.R.C.P.; 1938. London: H. K. Lewis and Company Limited. Demy 8vo, pp. 216, with 43 illustrations. Price: 10s. 6d. net.

The Medical Journal of Australia

SATURDAY, MAY 6, 1939.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction, are invited to seek the advice of the Editor.

THE MEDICAL RESEARCH COUNCIL OF GREAT BRITAIN.

THE report of the Medical Research Council of Great Britain for the year ended September 30, 1938, is a document of the greatest interest and importance. The council's ramifications are so far-reaching that a statement of the work carried out under its ægis in a twelve-month period gives the reader a good idea of the state of knowledge in most fields of medical research. Certain of the subjects are discussed in considerable detail, and some of these are mentioned in a special abstract which is published in another place in this issue. Apart from this, however, the report gives an insight into the methods of working adopted by the council, and so into the conception which its members have of its function.

The actual report of the Medical Research Council is preceded by a short report of the Committee of the Privy Council for Medical Research. In this preliminary report we are informed that for the year under consideration Parliament provided a grant-in-aid of £195,000. This included the sum of £30,000 specially provided (as in the previous year) for the development of research in chemotherapy. Administrative and other expenses of the council consumed £10,000. The sum of £60,000 was provided for the expenses, including salaries of staff, of the National Institute for Medical Research at Hampstead and of the farm laboratories at Mill Hill in association with it. For the salaries and expenses of scientific staff working elsewhere, including those in the units for clinical research maintained by the council in certain hospitals, those attached to various universities and other institutions, and those engaged in statistical inquiries or in work under the Industrial Health Research Board, a sum of £40,000 was provided. For temporary research grants to workers in various centres, for post-graduate studentships and research fellowships in clinical science and experimental pathology and for research fellowships in tropical medicine £55,000 were provided. The funds of the Medical Research Council have been augmented by donations from other sources too numerous to be mentioned in this place.

As it is twenty-five years since the Government of the United Kingdom decided to promote medical research by setting up the Medical Research Committee which later became the Medical Research Council, mention is made of the changes witnessed during that period. These twenty-five years will probably be pronounced by historians "as outstanding in the improved level of health of civilized communities made possible by the access of knowledge won by medical research". The whole face of medical practice has been changed, largely as a result of the development of radiology, biological chemistry and clinical pathology. Though this change has brought about an enormous increase in the cost of medical care, everyone will agree that it has been beneficial to humanity. But, the council asks, what is to be the end of this development? It also asks whether there is to be no limit to the size of hospitals and their scientific services. The economist may ask, as indeed some have already asked, whether a time will not come when the expense and trouble involved will justify further extension of medical practice, "especially that large

part concerned with chronic and degenerative forms of disease and for which the practical return in terms of human health is often small". Medicine, of course, can never adopt the point of view of the economist; its adherents must always use every means in their power to save and prolong life. Whatever the cold and calculating economist may think in the heyday of his professional youth and enthusiasm, he will no doubt alter his views if "chronic and degenerative forms of disease" attack his own person. The council in this connexion points out that the whole trend of medicine in the present century has been to study the basic ætiological factors of individual diseases. Many diseases which at the beginning of this century were treated merely by the relief of symptoms and the promotion of personal comfort, can now be cured and controlled by specific remedies. It is to the control of disease, in other words its prevention, that modern medical research is directed. The knowledge yielded by medical research, "if properly used, leads directly to the prevention and elimination of disease". The economist should be encouraged in the thought that the elimination of disease will reduce the need for expensive curative aids.

The statements in the report on the application of knowledge to preventive medicine are known to most medical men; we would that they could be disseminated among the general public. "Prophylaxis against disease does not depend solely on the alertness of medical men or of government departments to procure rapid application of knowledge." The enlightenment of the public is just as important. Unfortunately, though the cure of disease is always dramatic and brings with it intense relief to patients and to their friends, there is nothing dramatic about the disappearance of disease. "It is here today and gone tomorrow, and the very success of prevention of disease is measured by forgetfulness." Another reason why the discoveries of medical research workers are not more readily applied to the elimination of disease is that preventive medicine mostly concerns children, and, curiously, illness and death of the young "do not, apparently, impress themselves on the public mind with the emphasis associated with disease in the adult". The Medical Research Council makes these statements, but adds that it is not its duty to guide the public on the application of medical discovery to human needs. Its task is "wholly to promote discovery and to announce it to the world when it is made". This statement must be accepted. At the same time it must be emphasized that this report is the best possible argument that could be used for the practical application to communal life, with the least possible delay, of the discoveries made by research workers.

The policy of the council is of interest to Australian workers in view of the divergent views which have been expressed in this country on medical research. Reference is made to the contention that knowledge may be most quickly and effectively obtained by the direction of attention to the disease itself, and also to the view that fundamental studies of the physiology and chemistry of the body are more important. These views are not discussed, since experience has shown that experimental work from any quarter may lead to the solution of problems from any other quarter. Specific research is promoted by the council by the appointment of workers to its permanent staff. The worker selected has wide liberty of action in planning his investigation. Particular diseases are seldom chosen for investigation; a broader choice is generally made, so that an ætiological factor common to a group of diseases, or a type of treatment of wide application, or a system of physiological or biochemical control is included. Sometimes other workers in the same fields are assisted, and in this way effort throughout the country is coordinated. When personal or expense grants are made, the subject of investigation may be chosen by the head of a laboratory or institution or by the worker himself. It is important to note that the council does not provide money for institutions, but for individuals, because the council insists that it should retain direct control over the worker and his investigation. On account of the dearth of work in clinical science and experimental pathology, as compared with many other branches of medical science, the council is offering special scholarships and fellowships to enable young men and women to

take up this kind of work. It has been the duty of the council from its inception to help government departments in the elucidation of their problems in health and disease. The demands for such inquiries have during recent years become greater, and more and more time has had to be devoted to them by both the administrative and technical staffs of the council. The blunt statement is made that it would be idle to suggest that all these investigations have been undertaken with enthusiasm. This can be understood, for the investigations may be more or less of a routine or they may be difficult and time-consuming. Nothing is more harassing to a research worker than a demand for results when sufficient time has not been allowed for those results to be obtained. In these circumstances the best scientific work cannot be done. From this portion of the report we may draw a conclusion which it is most important that those who endow research and also the general public should realize: that a great deal of research work will always be unproductive of immediate results and that the intelligent worker who finds perhaps again and again that his work appears to lead nowhere, should not be frowned upon but encouraged to further effort.

Current Comment.

THE NUTRITIVE VALUE OF CANNED FOODS.

A SERIES of articles on matters concerning diet and nutrition is being presented by *The Canadian Medical Association Journal*. These articles are of particular value in view of the rapidly increasing use of canned or, as we largely say in Australia, tinned foods. Some authoritative guidance in their use is appropriate. L. B. Pett and M. M. Cantor have dealt with the nutritive value of canned foods.[1] They remind us that in early times smoking, drying or salting of foods was resorted to for their preservation. In present-day methods both low temperatures (freezing and refrigeration) and high temperatures (boiling and canning) are employed. In canning heat-processing of food is undertaken in closed containers. In 1775 Spallanzani showed that meat broth could be preserved if heated in corked glass bottles. Nicolas Appert, considering the problems arising out of the Napoleonic wars, was successful, in 1800-1810, in preserving an extensive number of foods by heat-processing in corked flasks. Between 1810 and 1840 the tinned iron container was developed in England and introduced to America. The pressure cooker was introduced about 1878, and heat-processing at temperatures higher than boiling point became possible. Automatic machinery was instituted from 1900 to 1910. In the canning process some selection of the raw material is made, followed by cleansing. Practicaly all products are subjected to some heat before being placed in containers. This may be merely a light scald or a prolonged boiling. Filling, along with brine or a syrup, is then effected into sterilized containers. This may be done while the product is hot and the container may be sealed immediately or later. There is generally a final sterilization by heating. Commercial canning is superior to home canning in the final steps, whereby all the air can be driven out and subsequent heating of the hermetically sealed can is more easily effected. Occasionally, but infrequently, tin, iron and lead (from solder) have been recorded in the contents; they have never been definitely shown to have been the cause of trouble. Further, there is no reason why the contents should not be left temporarily in the can, which is probably the most nearly sterile dish in the kitchen.

It is pointed out by Pett and Cantor that it is only in recent years that concern has been manifested concerning the food values of canned products. It is unhappily true that raw materials, even of the same grade, vary considerably in composition. Further, the effects of canning vary widely upon different constituents in the same food and even on the same constituent in different foods. Pett and Cantor insist that the only safe procedure in evaluating a foodstuff is to make analyses of raw, cooked and canned samples. They present a very extensive, but even then incomplete, table with analyses of foodstuffs in a raw, cooked and canned condition. This table indicates the caloric content, vitamins *A*, B_1, *C*, *D* and *G*, as well as calcium, phosphorus and iron. The term "pulped canned food" is employed to indicate food which has been comminuted, especially by its being forced through fine openings. Commenting upon the stability of vitamins under canning, Pett and Cantor remind us that vitamin *A* suffers only slight loss in canning, as it is fairly stable to heat in the absence of air. The loss varies between 10% and 50%, according to the product concerned, and is the same in the home as in the factory. Vitamin B_1 is appreciably destroyed in all cooking as well as canning. It is best preserved in acid products, the loss varying between 5% and 15%. When the product is alkaline the loss may be 80%. Vitamin *C* is notoriously the least stable of all the vitamins. However, owing to the occurrence of precursors or combined forms, it is perfectly stable to canning in some foods. It is entirely destroyed in other cases. Vitamin *D* is not of much importance in foods other than milk, in which it is fairly stable. Vitamin B_2 complex is perfectly stable to heat.

[1] *The Canadian Medical Association Journal*, February, 1939.

As regards the loss of minerals in canning, it is indicated by Pett and Cantor that iodine is lacking in canned foods, except sea foods, because canning districts are usually in goitre areas. Calcium and phosphates are precipitated in the canning of many foods. The precipitate is lost because it settles out or adheres to the metal or is insoluble in the gastro-intestinal canal. Most canned foods require to be heated again in the home. It has been advised that this be done in the can. This advice is rarely followed, with the result that further losses occur, mainly from oxidation.

Pett and Cantor conclude a valuable article by stating that the high standard maintained by manufacturers in the selection and handling of raw materials suggests the superiority of canned products over poor grades of raw products. They, however, advise reference to the actual analyses indicating observed losses of the particular food constituent under consideration. The additional cooking in the home of many foods entails further losses from the stated values; this has a tendency to bring the food value of canned products even lower than raw foods which are subjected to only one heat treatment. In the opinion of Pett and Cantor canned foods may in such circumstances be sometimes justified from considerations of price or convenience rather than of their food values.

THE DAMAGED LIVER.

IT is probably true to say that many medical men have no orderly conception of the functions of the liver. An orderly conception is necessary for the appreciation of disease, although the multiplicity and complexity of the vital processes which take place in this great chemical factory place complete understanding of them beyond even the physiologist and biochemist. Sir Arthur Hurst[1] has pointed out that deranged liver function, though commonplace, is frequently diagnosed as disorder of the stomach, bowels or nerves; but the patient is often unconvinced and is positive that his languor, sore head, coated tongue and distaste for breakfast are "liver, and the doctor be damned". Conversely, the "sluggish liver" is often one which has carried out its work of detoxication till it has been overwhelmed, and its disorder is consequent upon disorder of the alimentary canal, bile passages or spleen, or it may result from the ingestion of poisons or purgatives or toxiferous bacteria or protozoa. The liver is peculiarly subject to intoxication, and its cells, which are able to remove noxious substances from the circulation by altering them chemically or conjugating them with other constituents of the blood, are easily depressed in function or killed in the process; but the liver has also great powers of regeneration to replace damaged tissue, as witness the scarred livers with many nodules of new tissue which one sees now and then in cadavers. When intoxication of the liver occurs sufficiently to depress its function, symptoms of general intoxication are soon manifest, as on "the morning after the night before"; but when the liver is the seat of focal disease, so great is its reserve that functional depression sufficient to produce symptoms can be expected only when most of the organ has been destroyed. Nevertheless reflections of depressed function are often conspicuous as diminished tolerance of alcohol, lessened capacity to withstand surgical operations and infections such as pneumonia, or diminished coagulability of the blood. In addition there are many objective methods of demonstrating depression, and the more useful of these have been succinctly recapitulated by A. M. Snell and T. B. Magath.[1]

The liver is responsible for the secretion of bile, an alkaline liquid containing inorganic salts, organic constituents and various foreign substances eliminated from the blood. The most generally satisfactory test for hepatic function yet devised, according to Snell and Magath, who have an experience of over ten thousand tests, is made by a determination of the capacity of the liver to eliminate a dye, bromsulphalein, from the blood. The amount of dye still present in the blood is estimated colorimetrically one hour after the injection of five milligrammes of the dye per kilogram of body weight. Retention of more than four parts *per centum* is regarded as pathological. The test has particular value in the detection of metastatic cancer in the liver, retention of the dye to a significant degree occurring even when the metastatic deposits are "relatively moderate". The test is not used in the presence of obstructive jaundice, as the degree of retention of the dye, which is high, does not indicate the extent of the liver damage.

The liver excretes bilirubin from the blood into the bile. Bile bilirubin yields a "direct" reaction to the Van den Bergh test, blood bilirubin an "indirect" reaction. If the serum contains directly reacting bilirubin, this is good evidence of injury to the liver parenchyma, caused either by obstruction of the bile passages damming back the bile to the point of rupture of the capillary hepatic ducts, in which case jaundice will usually be present, or by damage to the liver cells, as often in arsenical poisoning, to such an extent as to allow the return of altered pigment to the blood, in which case jaundice may or may not be present. Serial quantitative estimations of the serum bilirubin may be of prognostic significance, high or rising values indicating complete obstruction of the bile passages or rapid degeneration of the hepatic parenchyma, or both.

The liver stores as glycogen carbohydrate absorbed from the intestine, and when lævulose is given by the mouth the normal liver can clear it from the blood as fast as it is absorbed. The damaged liver cannot do so, and the blood sugar

[1] *The British Medical Journal*, March 26, 1938.

[1] *The Journal of the American Medical Association*, January 15, 1938.

content increases. In the lævulose tolerance test, based on the researches of J. C. Spence and P. C. Brett,[1] suggested by H. MacLean, the blood sugar level is estimated in milligrammes per 100 cubic centimetres while the patient is fasting and one and two hours after he has taken 50 grammes of lævulose. If the sum of the differences between the fasting value and the other values exceeds 30 milligrammes *per centum*, this is regarded as certain evidence of hepatic insufficiency.

In the presence of jaundice some idea of the functional activity of the liver may be gained from a test of its detoxicating function, namely, that of A. J. Quick,[2] based on its capacity to conjugate benzoic acid and aminoacetic acid to form hippuric acid. In this test six grammes of benzoic acid are taken on an empty stomach and the urinary excretion of hippuric acid during the next four hours can be simply estimated and the result converted to terms of benzoic acid. Normal persons excrete the equivalent of 2·6 to 3·3 grammes of benzoic acid in the four hours. In "surgical" types of jaundice it is found that values of less than 1·5 grammes are associated with a bad prognosis.

Recently, L. J. Soffer, D. A. Dantes and H. Sobotka[3] have introduced a new test for hepatic function in the presence of jaundice, depending on the ability of the normal liver to clear sodium *d*-lactate from the blood within a short time by using it up to make glycogen. It would appear from their communication that the test is not a very sensitive means for the detection of impaired liver function, for in most cases of obstructive jaundice the liver is able to clear the blood of the sodium *d*-lactate injected; but the test could be used in the diagnosis of obstructive jaundice from jaundice due to intrinsic hepatic disease if the diagnosis were not made at the bedside or by other tests.

There has been of late an increasing realization in the consulting room and at the bedside of the importance of the recognition of derangement of hepatic function when it is present. Valuable biochemical aids to clinical judgement which have been developed abroad of recent years are still not widely accepted and employed in this country; but from an orderly conception of the functions of the liver it is but a step to their appreciation.

[1] *The Lancet*, December 31, 1921.
[2] *The American Journal of the Medical Sciences*, May, 1933.
[3] *Archives of Internal Medicine*, December, 1938.

THE COMMONWEALTH DEPARTMENT OF HEALTH AND ITS DEVELOPMENT.

IN April, 1939, there appeared a special issue of *Health*, which is the journal of the Commonwealth Department of Health. This issue is devoted entirely to an account of the development of the department and of its present activities. A prominent clinician, in discussing recently one of the newer medical organizations, said that anything in medicine which was for the whole of Australia was good. The Commonwealth Department of Health exists for the good of the whole of Australia; it has grown from very small beginnings and has been developed and directed along consistent and logical lines till at the end of thirty years its services embrace many activities and many important branches of national life. Under its Permanent Head, who is Director-General of Health and Director of Quarantine, there are 59 full-time medical officers and an allied scientific and administrative staff of 290 persons. It is appropriate, now that the department has reached its thirtieth birthday, that a short review of the recent issue of *Health* should be given, for too little is known of both the department's organization and its efforts to safeguard the health of the Australian people.

When the Commonwealth was established in 1901 quarantine was the only health power entrusted to the Federal Parliament under the Constitution; and it was not till 1909 that the Federal Quarantine Service was created. But, as *Health* informs us, "immediately and automatically" there arose the necessity for dealing with such matters as the giving of advice to the Customs Department on food and drugs, to the Treasury on pensions, to the Public Service Board on staff matters, and to other departments on questions connected with their work or with international relationships. The outbreak of smallpox in Sydney in 1913 and of war in 1914 created special problems, and among these was the fact that the importation of biological substances, such as serum and vaccines, might be stopped. The logical decision was to make Australia self-sufficient in this regard, and so the Commonwealth Serum Laboratories came into being. That these laboratories have been and are of the greatest value to Australian medical practitioners no one will deny; and the fact that Australia can if necessary supply all its own laboratory products is most important, particularly in these days of international unrest. In 1915 a committee was appointed to discuss ways and means by which the existing machinery for public health could be improved. Although this committee produced reports dealing with tuberculosis, infantile mortality, venereal disease and other matters, but little practical result followed. After the War, however, it became clear for various reasons that greater attention should be paid to health from the national point of view. The Commonwealth Government therefore decided in 1921 to meet the obvious necessity and determined to set up a full Department of Health; and its functions were defined by order in council in the following terms:

The administration of the *Quarantine Act*.
The investigation of causes of disease and death; the establishment and control of laboratories for this purpose.
The control of the Commonwealth Serum Laboratories and the commercial distribution of the products manufactured in these laboratories.
The methods of prevention of disease.
The collection of sanitary data and the investigation of all factors affecting health in industries.

The education of the public in matters of public health.

The administration of any subsidy made by the Commonwealth with the object of assisting any effort made by any State Government or public authority directed towards the eradication, prevention or control of any disease.

The conducting of campaigns of prevention of disease in which more than one State is interested.

The administrative control of the Australian Institute of Tropical Medicine.

The administrative control of infectious disease amongst discharged members of the Australian Imperial Force.

Generally, to inspire and coordinate public health measures.

Any other functions which may be assigned to it.

In 1925 the late Sir Neville Howse, then Commonwealth Minister for Health, secured the appointment of a Royal Commission, whose terms of reference were very wide and covered many aspects, particularly of preventive medicine. The report of the commission was and still is a most valuable document, setting out as it does the ideal to be attained in many fields of endeavour. (It was published *in extenso* in The Medical Journal of Australia of January 16, 1926). Many of the excellent recommendations of the commission could not immediately be put into effect; but one result was the creation in 1927 of the Federal Health Council. That this body achieved a large measure of coordination in public health activities as between Commonwealth and States is well known; and readers will remember how, comparatively recently, it was expanded and served as what we may call the foundation of the present National Health and Medical Research Council. The Royal Commission also advised that the activities of the Department of Health should be extended by the creation of special divisions. This was done and useful work was carried out. During the financial depression much of the work was unfortunately curtailed and some of the divisions disappeared. Now the Division of Veterinary Hygiene and the Division of Plant Quarantine alone remain. Divisions devoted to industrial hygiene and public health engineering have not been reestablished since State services in these spheres have been brought into being.

That our readers may be the more conversant with the activities of the Commonwealth Department of Health, mention will be made of some of the information set out in the special issue of *Health*.

We are told that Australia is now a party to more than three hundred treaties, conventions and other international agreements. Many of these deal directly with health; others are important from the medical point of view or carry implied obligations as far as health is concerned. Practically every activity of the department has now some international aspect. The quarantine code is based on Australia's acceptance of the International Sanitary Convention of 1926, and, for air traffic, of the International Sanitary Convention for Aerial Navigation of 1933. Under these conventions and under the Agreement of Rome, of 1907, Australia participates in the *Office International d'Hygiène publique* at Paris and in the epidemiological intelligence service maintained by that body with the Health Organization of the League of Nations and the Eastern Bureau of the Health Organization. Australia has a representative on the advisory council of the bureau, and its Director, Dr. C. L. Park, was formerly an officer of the Commonwealth Department of Health. Through the cooperation of the Royal Australian Navy the weekly wireless epidemiological bulletin, broadcast by the Eastern Bureau, is received each week and circulated to quarantine officers at all Australian ports. By its participation in the work of the Health Organization of the League of Nations, by its maintenance of a national centre for the international standards of biological substances, by its work on nutrition, on veterinary hygiene and plant quarantine and in other spheres the department is making a contribution on behalf of Australia "to that goodwill which is inherent in this technical cooperation between the nations, a spirit significantly free of those political and economic suspicions which cloud the outlook for international amity". The quarantine service has grown and there are now quarantine officers at 45 ports. At 14 major ports there are full-time quarantine officers of the Commonwealth Department of Health; at other ports local practitioners serve on a part-time basis. At 32 ports the necessary staff and equipment are maintained for inspection and "de-ratization" operations on ships. These ports are included as "qualified ports" in the list of 413 ports in 98 countries which cooperate in the international code. Major quarantine stations are maintained at five ports. Quarantine officers also act as inspectors under the Australian *Navigation Act* and regulations to see that the provisions of this act, which are extraordinarily complete, are observed.

The Commonwealth Serum Laboratories have a staff of 235 persons. Of these, 112 are permanent officers of the department. There are 31 university graduates and a large number of other skilled workers who have diplomas or qualifications from technical institutes. The laboratories are not, as may be supposed, devoted solely to the preparation and distribution of biological products. Much original and applied research is carried out within their walls, and papers of scientific value and importance by members of the staff have been published in this and other scientific journals. The laboratories are also the appointed national centre for the maintenance in Australia of the standards of the Permanent Commission on Biological Standardization of the League of Nations.

The Commonwealth Health Laboratories, situated at Darwin, Cairns, Townsville, Rockhampton, Toowoomba, Lismore, Bendigo, Launceston, Port Pirie, Kalgoorlie and Broome, are known to most medical practitioners in Australia. To those practising in their vicinity they have been indispensable. They are, moreover, centres of research, as is evident from many a valuable article by their officers published in this journal.

The history of the School of Public Health and Tropical Medicine has been traced in these pages on more than one occasion, and the Institute of Anatomy at Canberra is so well known that further reference need not be made to it.

The officers of the Division of Veterinary Hygiene deal mainly with quarantinable diseases in animals under the provisions of the *Quarantine Act*. The diseases mentioned in the act include glanders, farcy, *pleuro-pneumonia contagiosa*, foot-and-mouth disease, rinderpest, anthrax, Texas or tick fever, hog cholera, swine plague, mange, scab, scurra, dourine, rabies, tuberculosis, actinomycosis and *variola ovina*. To this formidable list 23 others have been added by proclamation. The work of the Division of Plant Quarantine is not less important than that of the division devoted to veterinary hygiene.

Among the other activities of the Commonwealth Department of Health are the organization for the control of cancer, the health services in the Australian Capital Territory, the Northern Territory Medical Service and work undertaken for other Commonwealth departments. The department also has certain responsibilities in the Pacific of national importance; it is concerned with the National Health and Medical Research Council and has recently taken a lively interest in physical fitness of the nation.

This short review of the work of the Commonwealth Department of Health will give medical practitioners some idea of what has been accomplished in the last thirty years. If they are discerning enough they will see running through the development of the department an aim and purpose which can best be described as directed to the protection of the health of the whole Australian people, that they may be worthy of their heritage and able to preserve it in health and vigour for future generations.

WHOLE SUPRARENAL GLAND IN THE TREATMENT OF ALLERGIC CONDITIONS.

THE allergic disorders of childhood are notoriously difficult to treat. Even when the allergen or allergens can be identified with certainty it may be very difficult to eliminate the offending substances from the patient's surroundings or from his diet; and a diet depleted of various common foodstuffs may be neither adequate nor appetizing. Eczematous rashes or bronchial asthma may entail constant misery for the afflicted child and endless anxiety and worry for its mother. Any method of treatment, therefore, which promises relief to these patients must be of great interest, even though it belongs to the highly debatable ground of endocrine therapy.

During the past eight years Orville E. Barbour[1] has administered whole suprarenal gland by mouth in the treatment of 380 children with disorders variously described as "allergic" or "vagotonic". He claims that by this method of treatment clinical improvement has been effected in 70% to 90% of these children. Desiccated whole suprarenal gland was used throughout this study in the form of uncoated compressed tablets. The products of several pharmaceutical firms were used. Most of them seemed to be satisfactorily potent if they were given when sufficiently fresh. Barbour observes that in acute conditions better results seemed to follow the administration of the adrenal gland at two-hourly or three-hourly intervals. Like those of epinephrine, its immediate actions appeared to be of relatively short duration. In more chronic conditions better results seemed to occur if the adrenal gland was given with the meals.

The most striking results were obtained in patients with infantile eczema. Barbour claims that a definite improvement usually followed within one or two days of the commencement of adrenal gland administration. He asserts that when the proper dosages for individual patients were attained, and if they were maintained, the skin condition remained under control in 80% of these patients. On several occasions when the endocrine treatment was discontinued the eczematous lesions shortly reappeared. In each case they soon disappeared again after the treatment with adrenal gland was resumed. Further, soon after the institution of the treatment the patients were enabled to tolerate with little or no skin reactions foods to which they were hypersensitive. It was easier, therefore, to supply the patients with an adequate diet, and case reports show that with the disappearance of the allergic symptoms there was an improvement in general health. Although he is convinced of the therapeutic effectiveness of whole suprarenal gland given by mouth in certain clinical conditions, Barbour admits that such treatment is quite empirical. The whole subject of endocrinology is in its infancy. It would not, however, be surprising if future work were to show that some endocrine deficiency or maladjustment underlies many of these allergic conditions. Allergic children are frequently of more than average intelligence, but their physical development is often retarded or is in some other way unusual, and the allergic condition often disappears if and when normal adolescence follows the changes of puberty.

[1] *Archives of Pediatrics*, November, 1938.

THE INSTITUTE OF MEDICAL AND VETERINARY SCIENCE, ADELAIDE.

THE recently constructed building for the Institute of Medical and Veterinary Science will be opened officially at Adelaide on May 24, 1939, by His Excellency Sir George Murray, K.C.M.G., B.A., LL.M., Lieutenant-Governor of South Australia. An address on medical research will be given by Dr. J. H. L. Cumpston, Director-General of Health, Commonwealth Department of Health. We join with others in wishing the institute and its director every possible success.

Abstracts from Current Medical Literature.

RADIOLOGY.

Pulmonary Fibrosis.

G. T. HEBERT (*Tubercle*, January, 1939) states that shadows due to tuberculous disease of the lungs are often interpreted wrongly as due to fibrosis, and conversely, that there is often a failure to diagnose fibrosis when positive shadows are lacking. A generalized peribronchial fibrosis, such as may accompany chronic bronchitis, can rarely be distinguished with certainty from a chronic inflammatory process without fibrosis; but the presence of general emphysema is suggestive inferential evidence. Coarse linear bands, especially if in the neighbourhood of an interlobar fissure, are more often due to an exudative process than to fibrosis; when they are due to fibrosis evidence of contracture is usually present. Neither density nor thickness of the wall of a round cavity can in itself be regarded as evidence of fibrosis.

Epiphyseolysis or Separation of the Capital Epiphysis of the Femur in Adolescence.

MAURICE M. POMERANZ (*American Journal of Roentgenology*, October, 1938) states that although the interpretation of skiagrams in early cases of epiphyseolysis is extremely simple, the radiologist too frequently fails to recognize the lesion. In the literature there is constant reference to the term "preslipping stage"; it is inaccurate to describe such a stage of the disease, since it does not exist. When clinical symptoms are suspicious, careful skiagrams, which must include a lateral view of the hip joint, will reveal some alteration in the epiphyseal line, the femoral neck or the head. The earliest stage of slipping can frequently be detected by the loss of the "hump" formed by the small projecting lip of the epiphysis, which normally extends slightly beyond the superior border of the femoral neck. The lower pole of the femoral head may project below the lower border of the neck in the form of a beak or small process. In the taking of the usual skiagrams the rays are projected through the thickest part of the epiphysis and produce an appearance suggestive of sclerosis, although no such change actually occurs. The apparent increase in the size of the head is due solely to its rotation on a vertical axis. The epiphysis remains within the acetabulum. In some cases the earliest evidences of disease are the alterations which occur at or near the epiphyseal line. Osteoporosis or resorption appears as a transverse band parallel to the epiphyseal line. The third sign is an increase in the width of the epiphyseal line. In the extremely early cases there is no perceptible alteration in the configuration of the femoral neck. The upper border of the neck adjacent to the epiphyseal line at this stage is simply freed from its attachment to the epiphysis and is noted as an irregular blunt projection. The femoral neck, however, is pulled outward and somewhat upward, as it is in fractures of the neck of the femur. The long-standing cases represent essentially the end results of preexisting slipping of the capital epiphysis. The idiopathic and traumatic cases cannot be differentiated. In the circumstances, therefore, the skiagram presents a variable picture, according to the extent of the original slipping or to the method of treatment employed. As a general rule the disease is self-limited and union invariably occurs. It is almost axiomatic that in most cases arthritis ultimately develops.

Visualization of the Heart and Thoracic Blood Vessels in Man.

GEORGE P. ROBB AND ISRAEL STEINBERG (*American Journal of Roentgenology*, January, 1939) state that visualization of the heart and thoracic blood vessels is a practical procedure. The method consists of the rapid injection of 25 to 45 cubic centimetres of a 70% solution of "Diodrast" into an arm vein, and the making of skiagrams when the chambers of the heart and the blood vessels are opaque to the Röntgen rays. "Diodrast" is a suitable radio-opaque medium, since it is freely miscible with the blood, rapidly eliminated, relatively non-toxic and inert, and non-irritating except at the site of injection in a few cases. The dose must be sufficient to make opaque enough blood to fill the right chambers of the heart and the pulmonary circulation at the same time, and, later on, the left chambers of the heart and the thoracic aorta. The delivery of "Diodrast" into the *vena cava* must be fast enough to produce a high degree of radio-opacity in the blood entering the heart, so that there may be an effective concentration after passage through the heart and the lungs. For visualization of the superior *vena cava* and the right auricle the time for exposure regularly is one and a half seconds after the beginning of injection. For the right ventricle and the pulmonary arterial tree the interval is usually three seconds, but may be six seconds or longer if pulmonary emphysema is present or if there is some other cause for slow venous inflow. In such cases the appropriate interval should be learned before injection by determination of the arm-to-lung circulation time and subtraction of one to two seconds. The frontal position is used for the study of the pulmonary circulation, the oblique position for the heart and the aorta. By this method it is possible to determine the site of stenosis or occlusion of the superior *vena cava* and its tributaries and the course and extent of the collateral circulation. The vascular nature of the hilum may be demonstrated, and these vessels may be differentiated from adjacent structures. The internal structure of the living heart has been revealed for the first time, and abnormalities due to disease have been observed. The following structures became visible: the superior *vena cava* and its tributaries, the four chambers of the heart, the ventricular walls and the interventricular septum, the tricuspid, pulmonic and aortic valves, the pulmonic and aortic sinuses, the pulmonary artery, and the entire thoracic aorta, including its wall and the branches from the arch.

Tumours of the Hypophysis Cerebri.

C. W. SCHWARTZ (*American Journal of Roentgenology*, October, 1938) states that a small glioma of the optic chiasma may present a serious problem in differential diagnosis. The *sella turcica* may be practically uninvolved; but the eye symptoms and findings will be very suggestive, and out of all proportion to the changes in the *sella turcica* if such symptoms are to be ascribed to a pituitary tumour. In addition, the optic foramina may well be enlarged unilaterally or even bilaterally. It is true that occasionally we find an optic foramen enlarged by a pituitary adenoma, but not until the *sella turcica* is considerably involved. Not infrequently encephalography will be necessary to prove the diagnosis; but in the presence of an optic chiasma glioma the distortions of the basal cisterns will not differ greatly from those produced by a suprasellar meningioma. However, the history and clinical findings will make the diagnosis. Rarely, a chiasmal glioma will undermine the anterior clinoids. This would not be expected in the presence of a meningioma.

The Radiological Diagnosis of Tumours Involving the Sacrum.

JOHN D. CAMP AND C. ALLEN GOOD (*Radiology*, October, 1938) state that, exclusive of metastatic processes, tumours involving the sacrum may be classified according to point of origin as follows: (i) tumours arising within the sacral canal, (ii) tumours arising from the body of the sacrum, and (iii) tumours arising from structures adjacent to the sacrum. The most common tumour arising within the sacral canal is the ependymal-cell glioma. This tumour causes erosion of the sacral canal by expansion and direct pressure. The margins of the eroded bones are sharp and well defined. Similar changes, which often are associated with erosion of a sacral foramen, are caused by neurofibromata. The most common tumour arising from the body of the sacrum is the chordoma. The most characteristic feature of the changes produced by a chordoma is the expansion of the sacrum by an infiltrative destructive process. It is often impossible to make a more specific diagnosis than "malignant tumour involving the sacrum" in cases of sarcoma, Ewing's tumour, metastatic carcinoma and

multiple myeloma. Teratomata are usually characterized by deformity or erosion of the sacrum by an extrinsic mass, in which may be seen teeth or calcification.

PHYSICAL THERAPY.

Lead Radon Tubules in Carcinoma of the Tongue.

F. E. SIMPSON (*Radiology*, October, 1938) describes a method of treatment for carcinoma of the tongue, minute lead tubules containing radon being used. The author has used this method since 1930. He does not favour the use of removable needles or seeds, and prefers the lead tubules to the more commonly used gold seeds. The length of the tubules is from 2·0 to 3·0 millimetres, the wall thickness 0·3 millimetre and the radon content 0·5 millicurie; 5% of antimony is incorporated in the lead to harden it. Prior to the implantation of the radon tubules a surface treatment is given to the lesion by means of radon tubes containing 500 to 1,000 millicuries attached to the end of a copper wire held in position for five minutes daily, till about 300 millicurie-hours have been given. This preliminary treatment reduces infection and shrinks the neoplasm. A biopsy is then made. The lead radon seeds are implanted in the tissue after block anæsthesia of the lingual nerve, and the actual insertion is carried out by means of a special introducer. The general plan is to implant the tubules in the form of a truncated cone, the smaller end towards the surface. The use of a fresh sterile needle for each puncture is advocated in order to obviate the possibility of the transplantation of cancer cells. The author reports the results obtained in 39 cases. Twenty-six patients had palpable lymph glands in the neck at the time of treatment and 13 had no palpable lymph glands. Six out of 26 in the first group are clinically well (though one is in poor condition); and 8 out of 13 in the second group are clinically well. Of the 14 who are clinically well, four have been well for over six years, one for over four years and three for over three years. The treatment of lymph glands in the neck is also briefly discussed.

Radiation Therapy in Primary Operable Rectal and Anal Cancer.

G. E. BINKLEY (*Radiology*, December, 1938), during the years 1925 to 1935 inclusive, has treated 65 patients with operable rectal cancer by radiation therapy alone. He states that radiation therapy is suitable for a fair percentage of operable cancers of the rectum as well as for the inoperable stages of the disease. The method which appears most suitable for operable rectal and anal cancer consists of external irradiation by means of either deep X rays or the radium bomb, in combination with the use of either (i) gold non-removable radon seeds or (ii) local radium applications given by means of a specially constructed rectal applicator. Of the 65 patients referred to, 34 were treated more than five years ago, and 17 of these (50%) survived for five years. Nine of them are still alive and have been clinically free of disease for periods varying from five and a half to ten years. Three died of intercurrent disease. The remaining 31 patients have been treated within the last five years. Twenty-three are alive, 21 having been clinically free of disease for periods varying from one year and three months to four years and six months.

Dosage in Radiation Therapy.

RALSTON PATERSON (*Radiology*, February, 1939) considers that progress in radiation therapy is being hindered by obsolete methods of prescribing and reporting dosage. He regards the three essential primary factors in any technique as being the following: (i) tissue dose, or the quantity of radiation absorbed; (ii) quality or wavelength of radiation; (iii) time or duration of treatment. As the *r* has already gained international acceptance, quantity in radiation therapy must be expressed in terms of this unit. The dosage system must determine the dose actually received at every point in a tumour, usually by the statement of maximum and minimum doses. The particular problems in the assessment of dosage in X ray and radium therapy are discussed. Paterson believes that the following terms of recording dosage should be discarded: *r* in air, erythema dose, summated *r* to skin fields, ergs per cubic centimetre and intensity-millicurie, milligramme-hours and millicuries destroyed. He gives three statements concerning dosage: (i) 4,750 *r* in eight days is a lethal dose to 80% of squamous-cell carcinomata; (ii) 8,000 *r* in ten weeks is a sublethal dose to the majority of squamous-cell carcinomata; (iii) skin tolerance, for a small area, ranges from just under 3,000 *r* in one hour to well over 10,000 *r* in ten weeks. One of the greatest needs of present-day radiation therapy is the development of such generalizations.

Röntgen Therapy for Inflammatory Lesions.

E. T. LEDDY (*Archives of Physical Therapy*, February, 1939) points out that the beneficial effects of Röntgen rays on inflammatory lesions has been known for many years, but the procedure has not received the recognition it deserves. Radiation therapy of inflammatory conditions is entirely different from that of tumours in that only moderate or small doses are used, which produce no harmful effects on normal tissue. In acute inflammation, the earlier the lesion, the smaller the dose required. A working rule is to give not more than 100 *r* for a very acute inflammatory lesion, for a subacute lesion about 100 to 150 *r*, and for a chronic lesion about 250 *r*. There are numerous acute lesions in the treatment of which the value of Röntgen therapy has been established. Among these may be mentioned furunculosis, carbuncles, cellulitis, erysipelas, pneumonia, gas-bacillus infection, acute *otitis media*, fibrositis. Provided treatment is given early, success follows in about 75% of cases. Among the chronic inflammations in which benefit is obtained may be mentioned tuberculous adenitis, actinomycosis, infectious arthritis in the early stages, and certain types of osteomyelitis.

Investigations in Fever Therapy.

F. H. KRUSEN AND E. C. ELKINS (*Archives of Physical Therapy*, February, 1939) have been particularly interested in modifications of the technique of fever therapy. They desired to increase both the safety of its application and the percentage of effective remissions in different diseases. They advocate, among other things, the following: (i) the intermittent use of oxygen and carbon dioxide during the session of fever to combat anoxia; (ii) the administration of one ten-hour session of fever instead of repeated six-hour periods; (iii) the application of additional local heat to the pelvis by diathermy in women with pelvic inflammatory disease of gonorrhœal origin; (iv) the intravenous injection of a 5% solution of dextrose in physiological saline solution before, during or after treatment, to lessen the danger of circulatory collapse; (v) the use of sulphanilamide in conjunction with fever therapy in cases of gonorrhœa resistant to treatment, in order to lessen the amount of fever therapy required.

Fever Therapy in Gonococcal Infections.

W. J. EGAN AND R. G. PIASKOSKI (*Archives of Physical Therapy*, August, 1938) point out that, in view of the bacteriologically established fact that the gonococcus is destroyed by temperatures within the limits of body tolerance, artificial fever therapy suggests itself as a logical procedure. They report on results obtained with 95 patients suffering from gonococcal infections treated during the period from December, 1934, to December, 1936. Of these patients, 60 were male and 35 female. The treatments were limited to four or five hours at a temperature of 106° to 107° F. The minimum number of treatments required was five at intervals of one or two days. The authors conclude that fever therapy will quickly and permanently cure gonorrhœa and its complications in over 90% of cases if the patients are willing and able to undergo adequate treatment. In its present form fever therapy is a strenuous ordeal, time-consuming, expensive and of necessity a hospital procedure, and it does not replace the routine treatment of simple uncomplicated gonococcal infection.

Special Abstract.

REPORT OF THE MEDICAL RESEARCH COUNCIL OF GREAT BRITAIN.

THE report of the Medical Research Council of Great Britain for the year 1937-1938 was presented to Parliament in February, 1939. Mention has been made of this report and of the general activities of the council in the leading article in this issue. The following is an abstract of some of the more important sections of the report.

The Treatment of Cancer by Radium.

In the section on the treatment of cancer by radium mention is made of the work on radium beam therapy, which was the subject of a special report. This report was considered in THE MEDICAL JOURNAL OF AUSTRALIA of March 11, 1939, at page 396. It is also stated that there looms in the distance the need for the study of the therapeutic effects of neutrons and of temporarily radio-active substances, such as radio-sodium, made possible by the discovery and development of the cyclotron by Lawrence in California. Reports indicate that the biological effects of neutrons are of even greater interest than those of X rays and γ rays. It is suggested that in cancerous growths and allied conditions, such as the leuchæmias, neutrons may be of outstanding importance. There is even a possibility that both radium and X rays will be superseded by the cyclotron in the treatment of cancer by radiations and radio-active substances. A member of the council's staff is at present working with Professor Lawrence in California.

Research on Hormones.

During recent years the advancement in knowledge of hormonal action has been so great that only experts can hope to keep abreast of the discoveries. The subject is not made easier to understand by the interaction of these substances one with another. The physiological action of these hormones also overlaps; this is seen in the sex hormones, for it is common to find female stimulating (gynæcogenic) properties in substances which are primarily male (androgenic) in action.

Some of the more interesting discoveries made during the year under review are mentioned, and among the substances described is synthetic œstrogen. Synthetic œstrogen (diethyl-stilbœstrol) was prepared by Dodds, Lawson and Robinson. Although it has some structural resemblance to the natural female hormone, œstradiol, it is considerably more active and is effective even when taken by mouth in small quantities. It can, moreover, be easily manufactured. At the request of manufacturing chemists the Therapeutic Trials Committee of the council has arranged to carry out extensive trials of its clinical value.

Parkes and Dodds have shown that this synthetic diethyl-stilbœstrol, when taken by mouth, inhibits the changes in the uterus which precede gestation, and that it thereby prevents or interrupts the implantation of the fertilized ovum in the uterine mucous membrane. It was found in rabbits and rats that daily doses of small quantities of diethyl-stilbœstrol given by mouth immediately after conception prevented implantation of the fertilized ovum in the uterus. In other experiments on rabbits it was found that oral administration of larger doses, but doses which were still small in terms of absolute quantity, could bring about interruption of pregnancy when once it was established. These studies are still in the experimental stage; but the council is careful to point out that there are possible detrimental effects and even dangers attached to the use of œstrogens and their synthetic derivatives for such purposes as those described. In inhibiting the progestational changes, they are capable, if given in excessive doses, of causing great hyperæmia and œdema of the endometrium of the uterus. The more remote effects of excess of these substances on the activities of the anterior pituitary lobe, with its controlling action on the functions of the sexual organs, are under investigation.

Reference is made to the administration of hormones by the subcutaneous implantation of tablets. Obviously any method of administration which reduces the number of subcutaneous injections necessary in hormone therapy or obviates their use, will be welcome. Deanesly and Parkes, working on animals at the National Institute for Medical Research, have found that a simple and effective method of producing prolonged action of hormones is to insert them under the skin in the form of crystals or compressed tablets. In these circumstances the substances are absorbed at a very slow rate and the effect of one tablet or crystal may be sustained for months or even years. From the experimental point of view the exact amount of the hormone used can be determined after any length of time by removal and weighing. Experiments of this kind are being made with œstrone, œstradiol, testosterone and testosterone proprionate, and also with progesterone and diethyl-stilbœstrol. The first clinical use of this method has been made by Bishop at Guy's Hospital. He found that a small tablet of œstrone relieved menopausal symptoms in a woman over a period of weeks. It is to be hoped that further clinical trials of this method will show it to be useful. At the same time it is pointed out that there is no evidence that hormones of a protein nature, such as insulin, show any advantage when given in this form.

Diabetes and the pituitary gland are discussed. We are reminded, as well we need to be reminded, that since the epoch-making work of Banting and Best in 1922 it is surprising how little more we know of the cause of diabetes or of the means of preventing its occurrence. Young, of the National Institute of Medical Research, has made experimental observations of great interest. In the course of an attempt to induce in dogs immunity to the so-called diabetogenic actions of extracts of the anterior pituitary gland, he succeeded in producing a condition of diabetes which continued permanently without further injections. The pituitary extract was injected daily, and at first some tolerance was established, but with progressive increase of the dose the tolerance disappeared and large quantities of sugar were passed in the urine, even when no further anterior pituitary injections were given. Young and Richardson found by histological examination of the pancreas of these dogs that the tissue of the islands of Langerhans showed changes varying from slight abnormality up to practically complete loss of cellular structure. Best and his co-workers at Toronto have also shown that in dogs rendered permanently diabetic by the anterior pituitary factor practically no insulin can be obtained by extraction from the pancreas and that no further significant change in the general condition or in the quantity of insulin required to prevent the excretion of sugar follows removal of the pancreas.

Young and Marks have made a study of the metabolism of these diabetic dogs. When they are given a high protein diet of lean meat the ingested protein is metabolized so as to give the maximum yield of glucose. This is excreted, the dextrose/nitrogen ratio in the urine being somewhat higher than in a dog from which the pancreas has been completely removed. If glucose is added to such a diet, it is quantitatively excreted, without any rise in the respiratory quotient. The dose of insulin required, on such a diet, to free the urine from sugar is certainly not less than that required for a dog without a pancreas under similar dietary conditions. The pituitary-treated dog on this diet appears by all tests to be completely diabetic; nevertheless it remains apparently in good health and vigour and retains its weight, even when no insulin is given. When such an animal is fed on a diet rich in carbohydrate, however, although it appears to metabolize some of this, excreting only 80% to 90% as sugar in the urine, it loses weight rapidly. When the diet consists almost entirely of fat, glucose added to it is largely retained, while the urine becomes free from sugar and almost from ketone bodies. These do not return with the addition to the diet of casein or of cooked and extracted meat, but immediately appear when raw meat

is given. The view is expressed that some of the facts discovered are of great scientific interest because they seem to extend previous observations on the relation of diet to the diabetic condition. The report goes on to state that one of the main difficulties in the understanding of the fundamental origin and cause of *diabetes mellitus* in man is the fact that the islands of Langerhans generally appear normal when the pancreas of a diabetic is examined microscopically after death. It is believed that insulin and therefore the tissue of the islands of Langerhans are the controlling factors in diabetes; but it is not known whether the diabetic condition is due to the liberation of too little insulin from the islet tissue or to interference with its activity after it has been formed. The interpretation of the work of Young and his colleagues is difficult. Only further work, in the opinion of the council, can decide whether the anterior pituitary function acts primarily by raising the threshold of sensitivity of the tissues against insulin or by a direct effect on the islet cells or by both mechanisms. The general conclusion is that the study of diabetes in man is now open to a new line of attack.

The Physiological Actions of Alcohol.

A relatively large section of the report is devoted to what is in effect a review of the third edition of "Alcohol: Its Action on the Human Organism". This book has been out of print for some years, and the third edition has been published as a result of the steady demand for it. There is an interesting discussion of two popular fallacies which are exploded in the book: first, that alcohol is a stimulant, and secondly, that it has a warming effect on the blood and tissues when taken after exposure to cold. The parts of the book dealing with chronic alcoholic intoxication have been rewritten, and it is for this reason that the book is mentioned in this abstract. Reference is made to the work of Wechsler, Minot, Strauss and Cobb, Joffe and Joliffe and others, who have shown that the form of peripheral neuritis commonly seen in chronic alcoholics is due not, as was formerly supposed, to a poisonous action of alcohol on the nerve tissues, but rather to deficiency of vitamin *B*, especially of vitamin B_1, in the alcoholic's diet. So-called alcoholic neuritis is thus to be regarded as a nutritional disorder closely related to beri-beri. There is also some evidence that some other morbid effects of chronic alcoholism, such as gastric changes and the "alcoholic heart", may be due at least in part to vitamin B_1 deficiency. The significance of this work as far as treatment is concerned is obvious; but perhaps of more importance is the method by which alcoholism may lead to harmful effects in the tissues. Probably decreased intake of vitamin *B* is one of the factors responsible—the alcoholic as a rule has a poor appetite; he can obtain his working energy from alcohol instead of from other foods, and in these circumstances he may use more vitamin. It is stated that workers in Great Britain have only comparatively rarely been able to obtain with the vitamin the dramatically rapid cures reported by some workers in America.

Physical Training.

In the leading article in this journal in the issue of April 29 mention was made of the Physical Exercise Research Committee appointed by the Medical Research Council. The members of this committee are: Sir Henry Dale (chairman), Professor E. P. Cathcart, Lord Dawson of Penn, Professor A. Hemingway, Professor A. V. Hill, Professor B. A. McSwiney, Sir Edward Mellanby, Professor H. S. Raper and Dr. F. J. C. Herrald (secretary). This committee has considered the accommodation and facilities required for the teaching of physiology and anatomy at the proposed National College of Physical Training. In association with the committee on physical training set up by the Health Organization of the League of Nations, the committee of the council has drawn up a form of standardized medical examination, to be used especially for students at universities, which will provide a comprehensive record of the results of physical examination. The main work of the committee will be to advise the council on matters relating to the planning and initiating of investigations on questions of physical exercise and its relation to health, both at the National College of Physical Training and at university and medical school centres.

Pulmonary Disease and Industry.

The problem of chronic pulmonary disease among coal miners was brought before the Medical Research Council by the Home Office and the Mines Department. After a committee of the council had recommended that thorough scientific investigation should be undertaken in order to obtain new knowledge on which methods of prevention and treatment could be based, the council accepted the responsibility of doing so. Investigations started in 1936 and are still being carried on. The council insists that research of this kind is necessarily slow and that public interest in the subject, shown by numerous questions in Parliament and in the Press, cannot accelerate its progress. Workers at a colliery in South Wales have been thoroughly examined and these will be compared with those from other collieries. No indication is given of what the findings are likely to be; but it is stated that possibly new information will be yielded when all the evidence is available for review.

In the Department of Tuberculosis of the Welsh National School of Medicine, Cardiff, Professor S. L. Cummings and his colleagues have made an interesting experimental inquiry into the nature and extent of the lesions induced by the prolonged inhalation of sandstone, slate and anthracite dusts, with and without simultaneous inhalation of killed tubercle bacilli as a source of tuberculous toxins. Preliminary results have indicated that the dusts produced much more pronounced lesions when inhaled with the dead tubercle bacilli than alone, and that the sandstone (obtained from the colliery investigated) was more injurious than slate dust. These findings will be analysed when some confirmatory experiments with anthracite and sandstone dust are completed. It is interesting to note the insistence of the council that the administrative problem as to whether chronic pulmonary disease among coal miners should be scheduled as an occupational disease under the *Workmen's Compensation Act*, along with silicosis, is outside its province. This investigation is possibly one of those which the council has undertaken "without enthusiasm"; but in more than one place in the report it acknowledges the helpful cooperation given in connexion with it by the Home Office, the Mines Department, the mine owners, the workers, various other workers and independent experts.

Epidemics in Schools.

In 1929 the council appointed a committee to inquire into the prevalence and mode of spread of minor epidemics in residential schools. During the past year an interim report has been published on this subject. The committee found at the beginning of its inquiry that about half the children in the school population under survey had had their tonsils removed and that this proportion increased through the years of observation by more than 6%. It was thus important to discover if possible whether this mass attack on what is a normal structure in the body was justified. The conclusion is that its justification is doubtful. The incidence of naso-pharyngeal infections, such as "influenza", colds and sore throats, upon boys and girls with or without tonsils, did not differ. In a group of 364 boys whose tonsils were removed during school life, the sickness experienced before removal of tonsils was worse, and after removal was about the same as that of the population as a whole. "This shows, what expert clinical experience supports, that in selected cases the operation is of value; but it is far from justifying a ritual now practised upon more than fifty per cent. of the children admitted to schools of this class." Investigation revealed a remarkable difference of incidence of illness between boys and girls—a problem which awaits solution. Boys, as compared with girls, were found to suffer twice as frequently from middle ear disease, two and a half times as frequently from pneumonia, and eleven times as frequently from acute rheumatism. Though this may be a

real sexual difference, it is pointed out that the difference may be due in part to a stricter supervision of girls and earlier isolation of the sick. Moreover, contacts in girls' schools, where cubicles or separate bedrooms are more usually found than in boys' schools, may be less close.

On the wider scientific problem of the factors which determine whether a disease in a community shall become epidemic, the data so far assembled are insufficient to justify the drawing of general conclusions.

Virus Diseases.

In last year's report reference was made to the new evidence that the strains of virus obtained from different outbreaks of epidemic influenza were not all of one antigenic type, but of a number of different types. It was thought possible that the position might be analogous to that which had been revealed by investigation of the pneumococci. Andrewes and Wilson Smith have been following up this type of study. They find that certain strains of the virus can be clearly distinguished from one another by their antigenic properties, as shown by the neutralizing action of corresponding immune serum. These specific strains fall into four main antigenic types, which by themselves would provide an analogy to the types of pneumococci. There are, however, other strains which do not show such a sharp type specificity, but which appear to react with the immune serum evoked by all strains of the human influenza virus. In addition to these type-specific and "master" strains, there are others of intermediate type, neither so specific as the former nor so polyvalent as the latter in their antigenic reactions. The council points out that the preparation of an effective vaccine for the production of immunity in advance against an expected epidemic of influenza is not a simple problem. The available knowledge, however, has enabled a number of experimental comparisons to be made of the immunizing potencies for mice and ferrets of vaccines prepared from specific, polyvalent and intermediate strains of the virus, and also of the vaccines made from any strain by killing or inactivating it by different methods. The results of these investigations are to be published; and we are told that the next practical step will be the trial on a human community of the protective effect of a vaccine prepared by methods which seem most likely to be effective in conferring immunity to any strains of virus which may be encountered, including such as are not specifically represented in the vaccine.

Lung Cancer and Dust.

In previous reports reference has been made to experiments carried out by Campbell on the effects of life-long exposure of mice to various kinds of dust. The soot from exhaust pipes of heavy oil motors used on certain public vehicles has been thoroughly tested. No evidence of any important carcinogenic properties has been obtained, although the incidence of lung tumours in mice inhaling it was somewhat greater than in the normal controls. Although a carcinogenic tar can be artificially extracted from soot from a domestic coal fire chimney, this soot, when inhaled as a dust, causes only a small increase in the incidence of lung tumours in comparison with the increase caused by dust from tarred roads. The conclusion is that probably the action of organic carcinogens in a modern road dust must be reinforced by some properties of the mineral basis; the chemical examination of various mineral dusts which have been associated with a high incidence of lung cancer in man suggests an association of silica and iron oxide as a common feature of their composition.

Clinical Research Units.

From time to time mention has been made in this journal of the clinical research units established at teaching hospitals in different parts of the United Kingdom. One section of the report is devoted to a short description of work done at these units. Sir Thomas Lewis, well known for his work in "clinical science", is director of the unit at University College Hospital, London; Dr. R. T. Grant is in charge at Guy's Hospital; Dr. E. Arnold Carmichael at the National Hospital for Diseases of the Nervous System, Queen Square, London; and Dr. W. C. Wilson at the Royal Infirmary, Edinburgh. In addition to the description of work done at these units, a list of papers published by workers is given.

Other Researches.

Many pages of the report are filled with descriptions of work begun, completed or in progress at various centres by members of what are known as the external scientific staff or by workers who receive scholarships, fellowships or grants to assist them in their work. Much of what is written in regard to these researches is of absorbing interest. To mention the subjects under investigation would be to refer to practically the whole range of medicine. A great deal of the work is necessarily incomplete; and those who are interested in a particular field of medical science are advised to study this report together with some of its predecessors.

Public Health.

THE SERUM PROPHYLAXIS OF MEASLES.

THE following preliminary note on the serum prophylaxis of measles, by Dr. Hilda W. Bull, of the Department of Health of the Melbourne City Council, is published at the request of Dr. John Dale, Chief Medical Officer of the department.

In common apparently with most of eastern Australia, Melbourne has been awaiting the reappearance of measles after an absence of nearly three years.

Early in March a number of cases were reported and it was discovered that infection had been introduced in a small kindergarten in North Melbourne early in February, as measles cases of the third generation were then appearing among the children. It was decided to make extensive trial of the use of pooled adult serum and of convalescent serum, if obtainable, in order to protect as many as possible of those young infants and of weakly children who would be exposed to the disease.

During former prevalences considerable use had been made of serum prophylaxis, both convalescent and pooled adolescent sera being used with encouraging results, particularly in institutions; but in the absence of notification of the disease the numbers of children treated in their homes had been small.

All schools and kindergartens were reminded of the existing arrangements to notify absences of scholars on account of measles or of doubtful sickness, and a pamphlet was prepared, describing the symptoms and notifying parents of the possibility of serum prophylaxis for younger children. A few days later, when it became apparent that the disease was widespread in North and West Melbourne, the help of the Press and broadcasting services was enlisted. Before the Easter vacation of the schools pamphlets were given to all children to take home.

Up to the time of writing, the disease has been almost confined to the North and West Melbourne areas of the city, where it is estimated that there are approximately 1,750 children aged under five years, and it seems that a majority of the families have become infected. Excluding the work in institutions, serum has been administered to 60 young children in homes, and results are already ascertainable in relation to 50 of these. Twenty-six appear to have escaped infection altogether and 27 have developed the disease. All these latter have had mild attacks, and only two could even be described as typical. In the majority of instances there have been practically no constitutional symptoms, and had it not been for the presence of the rash the infection might have passed unnoticed. Parents are emphatic in asserting that the sickness of the treated child has been much milder than in the

original or infecting cases, and are grateful for the service rendered.

In the majority of instances the rash appeared in the inoculated children between the ninth and thirteenth days after the rash of the infecting case, though in several instances the incubation period seems to have been prolonged, as is apparent from Table I.

TABLE I.

Interval between Appearance of Rash of Presumed Infecting Child and of Second Case.

Number of Days.	Number of Children
9	4
10	5
11	5
12	3
13	4
14	1
15	—
16	1
17	—
18	—
19	—
20	—
21	—
22	1

In two cases only one day and in one five days intervened. The number of cases was 27.

Where incubation appears to have been prolonged it is not known whether reexposure to infection took place, but parents were warned to avoid it as far as possible. In the instance of the 22-day period no history of such exposure could be discovered and the possibility of reexposure seems to be excluded.

As a rough control of the above series details have been ascertained of the history of 44 younger children, exposed in homes to infection from older children, who did not receive serum either because of the objection of parents or because the situation was discovered too late. Of 44 such children, four appear to have escaped infection and 40 developed the disease. Eight of these 40 are recorded as having had severe attacks, and complications noted include bronchopneumonia in five instances, severe bronchitis in one, and severe conjunctivitis in another.

The ages of the children treated are shown in Table II.

TABLE II.

Age.	Number of Children.
0 to 6 months	1
6 to 12 months	2
12 to 18 months	9
18 to 24 months	9
2 years	8
3 years	8
4 years	12
5 years	3
6 years	1

The serum used has been pooled adult serum of the Commonwealth Serum Laboratories, and the dose given has varied according to the size of the child and the intention either to prevent altogether or to modify the attack.

Children have received doses as follows: Fifteen children received 10 cubic centimetres, 20 children received 15 cubic centimetres, and 18 children 20 cubic centimetres.

The serum has been injected subcutaneously into the anterior abdominal wall and no trouble beyond a transient discomfort has been experienced. The time which has elapsed between exposure, dated from the apearance of the rash in the infecting child and the giving of serum to the exposed child, has been as shown in Table III.

The weather during the period has been for the most part warm and sunny, and during the several days of rain

TABLE III.

Interval between Appearance of Rash in Presumed Infecting Case and Injection of Serum.

Number of Days.	Number of Children to whom Serum was Given.
0	8
1	17
2	18
3	5
4	3
5	2
6	—
7	—

the temperature has remained high. Perhaps on this account the disease has been relatively mild without complications in the majority of instances. A considerable amount of bronchitis and particularly of gastro-enteritis has nevertheless been encountered during the preliminary or prodromal period, and a number of patients have been admitted to hospital with bronchopneumonia and enteritis. Two deaths have occurred, in one case from an institution and in another from a home in North Melbourne, from complicating enteritis and pneumococcal meningitis respectively. Amongst those who have received serum, however, there have been no complications and, as stated, almost an absence of prodromal symptoms. It seems, therefore, that the use of the serum is well justified, and this preliminary note is published in order to encourage its further trial.

Correspondence.

GROUP PRACTICE.

SIR: Going back almost to ancient history, I should like to express my appreciation of an article in THE MEDICAL JOURNAL OF AUSTRALIA of January 21, 1939, by Dr. L. J. Jarvis Nye, on group practice.

As he says, when the trend in medicine is swinging naturally or being forced in any direction, it is wise to study the end of that trend and so to direct it in its course that the best results may be obtained. It is none too soon to make sure that we have some sound and unbiased ideas on the subject and that the profession as a whole is able to give the answer, if required, that will be in the best interests of the people whom we profess to serve.

There are several points about group practice which to me, in my inexperience, seem to need clarification, and I would be pleased if he (or any other) would see fit to amplify them for me.

1. Does the general surgeon largely supervise the surgical efforts of the general physicians or have them to assist him in their own cases where beyond their scope, or does he do all the surgery himself?

2. Does the general physician stand in relation to his patients as does a "family doctor", in so far as it is consistent with free choice by the patient within the limits of the group? That is to say, maintaining the contact with and confidence of all the members of the family and being in a position to advise them on all matters of physical and mental health, and as far as possible establishing a continuity of care for a long time.

3. Group units appear to me to form a wonderful medium for continuous and organized post-graduate education. By means of short "tutorials"—daily if possible—carefully prepared and printed, presenting all that is certain and of significance in recent advances, as well as steady revision of past knowledge, the professional education of doctors could be maintained at a very high level. Some of this could be prepared as a standard throughout the country or Empire, and some, of course, would be

adapted to local needs. In this way keeping abreast of modern medicine as well as polishing up old truths could be made as perfect and as easy as possible.

4. The medical man should not be placed in the possible position of adopting standards of interest and treatment which might vary with the financial status of the patient or with his own prospects of remuneration, thus avoiding the temptation of unnecessary operations for commercial gain. Nevertheless, the remuneration of the general physician at least should, to a certain extent, be on a *per capita* basis. Furthermore, it seems best suited to the most efficient practice of medicine that patients attending the group clinic should pay a certain fixed yearly sum according to income, and also a very small amount per visit, again proportionate to their income and ability to pay. This tends to curb those few who, getting something for nothing, become a plague to the doctor by too frequent visits. It also eases the conscience of those who feel guilty about wasting the doctor's time and giving him nothing for it—a larger group. Still more important, it clears the way for those people who are deterred from attending in any illness until they are so bad they can no longer stay away because 10s. 6d. seems a big sum to them. It is this factor as much as any other than has militated against early diagnosis in those insidious diseases where all hope lies in finding them in time. The payment per visit should be largely independent of the treatment adopted. This is easily obtainable in a large clinic, where the risk can be spread.

5. To what extent would it be possible to apply group practice in country districts?

6. What other tests are done as a routine besides a Wassermann test or its equivalent? A Mantoux, for example, in those under 30?

7. How does group practice affect the visiting of patients in their own homes, if at all?

8. If a group is not attached to a hospital, what proportion of beds for observation *et cetera* is needed? It seems that a hospital would naturally tend to spring up wherever a group was functioning.

9. And finally, is it possible and advisable to encourage all patients to report at specified intervals, that is, annually or more or less frequently, for a general check over, even if they feel in the best of health; and similarly, are groups used for systematic education of the people in health matters?

I hope that Dr. Nye will throw light on at least some of the queries here set down; and I would like to round off with the opinion that, if a fair proportion of practitioners took that intelligent and open-minded attitude to possible avenues for improving our service to the people as he does, the status and honour of the profession would be elevated even beyond the high position that now it holds.

Yours, etc.,

A. McQueen Thomson.

Balaklava,
South Australia,
April 1, 1939.

A BITE BY ATRAX ROBUSTUS.

Sir: I received an urgent summons to attend to a male patient, aged fifty-five years, who had been bitten on the hand by a large spider.

Upon my arrival the patient was standing in the garden, and at his feet was the dead body of a large black spider. On the palmar surface of the terminal phalanx of the ring finger of his left hand was the puncture of the spider. The patient's face was mask-like, the eyes staring and pupils dilated, the corners of his mouth drawn up, his appearance suggesting the *risus sardonicus*, and in addition profuse salivation was present and he was executing short dancing steps, the so-called "tarantism" or hysterical impulse to dance of the Italian writers.

He did not complain of pain, but of a marked salty taste in the mouth, and on getting him to bed the movements ceased. I applied to the site of the bite a paste of ammonia and bicarbonate of soda, and ordered hot bottles to extremities and copious drinks of hot freshly infused tea.

Within twelve hours he felt well, but very stiff and sore all over, and within forty-eight hours was able to take the corpse of the spider to the Government entomologist, who identified it as *Atrax robustus*, the deadly trapdoor spider, whose bite is sometimes fatal.

I have treated many cases of spider bite, including the red-back, the small black spider, and the large *Lycosa godeffroyi* or garden wolf-spider, but have never encountered the phenomenon of "tarantism" before.

Yours, etc.,

A. M. Watkins, M.B., B.S. (Melb.).

Roseville,
New South Wales,
April 6, 1939.

THE HOLGER NIELSEN METHOD OF RESUSCITATION.

The following copy of a letter from Mr. A. C. P. Handover, Vice-President of the Royal Life Saving Society, London, has been forwarded for publication. A report of the demonstration before the Victorian Branch of the British Medical Association, referred to in the letter, will be found in The Medical Journal of Australia of January 8, 1938, at page 84.

14, Alexandra Gardens,
Hounslow,
Middlesex, England,
January 5, 1939.

E. A. Pleydell, Esq.,
Hon. Secretary,
Victoria Branch,
Royal Life Saving Society.

Dear Mr. Pleydell,

On turning out my papers at the end of the year I came across a letter from you, sent on to me by Captain Biscoe under a covering letter from him of the 14th June, 1938. In this letter, which refers to your demonstration of combined Schafer pressure and Holger Nielsen lift before the British Medical Association, Victorian Branch, in November, 1937, you ask, "I would like to hear what Mr. Handover thinks regarding this matter".

With reference to this point in connexion with the full report in The Medical Journal of Australia of January, I spoke in some detail at the July meeting of our Central Executive. Recently I had a talk with Captain Biscoe and we came to the conclusion that I ought to write to you expressing my views, in case he had not conveyed them fully.

From correspondence with Colonel Holger Nielsen he states that the combined method you have tried was one stage in his investigations, but that he discarded it because it was a two-man method. This feature he regarded as rendering it generally unsuitable for first-aid work, as frequently only one skilled operator would be available. This view he confirmed when he gave me a demonstration and a discussion of his method during a visit I paid him at Copenhagen, Denmark, in August, 1937.

News had also reached me that Prof. C. K. Drinker, of Harvard University, U.S.A., had been conducting a series of experiments with this combined method during 1935. On receipt of your news I therefore wrote to him, because no published account of his results had come into my hands. Relevant paragraphs were:

> Recently interest has developed among our Australian workers in the possibility of the use of a combined Schafer pressure and Holger Nielsen lift. But this requires two operators for its success . . .
>
> Would you please indicate if your results have yet been published and how a copy can be secured; or

your opinion at this present stage of its usefulness as a first-aid measure in any of the varying circumstances in which need for resuscitation arises.

To this he replied by a signed letter of the 8th July, 1938, a copy of which I am enclosing. The answer is quite definite and confirms the opinion expressed by Prof. Crowden (Dept. of Applied Physiology, University of London), who stated, concerning this combined form of resuscitation, "It would not be desirable to ventilate the lungs to this extent except possibly in the early stages of carbon monoxide poisoning". (Amsterdam lecture, 1936.)

A later view incidental to this matter is expressed by Prof. Yandell Henderson, of Yale University, U.S.A., in his new book (Sept., 1938), "Adventures in Respiration", where he says:

> Another observation of high significance made during our work with the rebreather, and mentioned above, was the extent to which the consumption of oxygen in the body is independent of the supply. It has been long known that a man breathing pure oxygen consumes no more than when breathing mere air, containing only 21% of oxygen. But it was not realized that the same rate of consumption continues even into extreme anoxia.

Thus to increase the ventilation of the lungs abnormally with a view to increasing the quantity of oxygen available for use in the tissues is a fallacy, since the body will absorb just the quantity it requires and will discard the rest. And this is true whether the supply of oxygen is great or small.

Other experimental work under his supervision proves the same point, as (p. 273):

> To determine the efficiency of the various methods of artificial respiration, I introduced them into the work of the students in my laboratory course. In particular the prone pressure method was applied to each student by another, and compared with other manual methods. The volume of the pulmonary ventilation induced was measured by means of a close-fitting mask, from which the expired air passed to a gas meter. We found that the volume of air, thus artificially breathed, was in all cases and by all methods, if continued long enough, almost exactly the same as that of natural breathing: never appreciably more, never appreciably less.

Later also he states (p. 276):

> Evidently it is the state of the subject, not the technique of the operator, that determines the volume of artificial respiration, as Liljestrand also found. All the tests of the various alleged improvements on the Schafer methods, and on other methods, that have been made on men in normal condition, with normal respiratory centres and normal tonus, are valueless as evidence of the comparative merits of these improvements and methods. All such tests on normal men would, if continued for 10 or 15 minutes, give an exactly normal pulmonary ventilation.

Interesting, as a finale, is the following (p. 275):

> It was my conclusion 25 years ago, and on the basis of much experience, since it is my opinion still, that . . . the Schafer method does all that it is possible to do by means of manual respiration. It is impossible by any manual method to induce a greater degree of respiration than the tonus of the patient's own muscles produces. The claims that other methods do more for respiration are all fallacies, because based on observations on normal men. The prone pressure method is most easily applied, and can be continued longer than any other procedure. It is therefore best. It also aids the circulation by pressing blood from the abdominal vessels toward the heart.

Thus, you see, results of practical experiments at present show that there is no method superior to Schafer's, viewed in all the aspects requisite in first aid. It has appeared to me to be wiser to deal with the comparative values of method by quoting from these many external authorities than by merely reiterating the society's claim for Schafer or just expressing my personal ideas of its outstanding value for our work.

Yours, etc.,
(Sgd.) A. C. P. HANDOVER,
Vice-President,
London. Royal Life Saving Society.

Harvard University,
July 8th, 1938.

Mr. A. P. Handover,
14, Alexandra Gardens,
Hounslow, Middlesex,
England.

My dear Mr. Handover,

We have had some opportunity to try out the combination of the Schafer and Nielsen procedures and see nothing in it which causes us to continue to experiment. We therefore have returned to the simple Schafer method without modification of any sort. This covers not only gas poisoning but electric shock and drowning.

Very sincerely yours,
(Sgd.) CECIL K. DRINKER, M.D.,
Dean and Professor of Physiology.

The Royal Australasian College of Surgeons.

MEETING OF THE BOARD OF CENSORS.

THE next meeting of the Australian Board of Censors of the Royal Australasian College of Surgeons will be held at the college, Spring Street, Melbourne, probably in August, 1939.

Candidates who desire to present themselves at this meeting should apply to the censor-in-chief for permission to do so, on or before June 30, 1939. The appropriate forms are available at the college, Spring Street, Melbourne, and at the offices of the various State secretaries.

Research.

SURVEY OF PNEUMOCOCCAL INFECTIONS: AN APPEAL.

THE survey of pneumococcal infections which was commenced last year at the Kanematsu Memorial Institute of Pathology, Sydney Hospital, will be continued during the coming winter. The cooperation of medical practitioners in submitting specimens of sputum from patients with pneumonia will be greatly appreciated.

Specimens, with clinical diagnosis and details of the patient's name and age, may be left with the gate porter at Sydney Hospital, Macquarie Street, or will be collected by messenger if Miss Stobo, First Floor, Pathology Department, Sydney Hospital, is notified. The telephone number of Sydney Hospital is BW 1291.

Obituary.

WILLIAM PATRICK KELLY.

WE regret to announce the death of Dr. William Patrick Kelly, which occurred on March 30, 1939, at Sydney, New South Wales.

HENRI VICTOR DAVID BARET.

We regret to announce the death of Dr. Henri Victor David Baret, which occurred on April 19, 1939, at Lidcombe, New South Wales.

ARTHUR ERNEST TAYLOR.

We regret to announce the death of Dr. Arthur Ernest Taylor, which occurred on April 28, 1939, at Dandenong, Victoria.

Nominations and Elections.

The undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Sharp, Alan Cathcart Ritchie, M.B., B.S., 1938 (Univ. Sydney); Sydney Hospital, Sydney.

Diary for the Month.

May 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
May 11.—South Australian Branch, B.M.A.: Council.
May 12.—Queensland Branch, B.M.A.: Council.
May 16.—New South Wales Branch, B.M.A.: Ethics Committee.
May 17.—Western Australian Branch, B.M.A.: Branch.
May 18.—New South Wales Branch, B.M.A.: Clinical Meeting.
May 23.—New South Wales Branch, B.M.A.: Medical Politics Committee.
May 24.—Victorian Branch, B.M.A.: Council.
May 25.—South Australian Branch, B.M.A.: Branch: Listerian Oration.
May 25.—New South Wales Branch, B.M.A.: Branch.
May 26.—Queensland Branch, B.M.A.: Council.
June 1.—South Australian Branch, B.M.A.: Council.
June 2.—Queensland Branch, B.M.A.: Branch: Joseph Bancroft Memorial Lecture.
June 6.—New South Wales Branch, B.M.A.: Organisation and Science Committee.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser", pages xx to xxii.

Australian Aerial Medical Services, Sydney, New South Wales: Medical Officer.

Department of Public Health, Melbourne, Victoria: Resident Medical Officer.

Lewisham Hospital, Lewisham, New South Wales: Honorary Officers.

Mackay District Hospital, Mackay, Queensland: Assistant Medical Superintendent.

Royal Australian Air Force: Medical Officers.

Royal Hospital for Women, Paddington, New South Wales: Resident Medical Officer.

Surat District Hospital, Surat, Queensland: Medical Officer.

Tambo Hospitals Board, Tambo, Queensland: Medical Superintendent.

The Broken Hill and District Hospital, Broken Hill, New South Wales: Resident Medical Officer.

The Women's Hospital, Crown Street, Sydney, New South Wales: Honorary Assistant Urologist.

Tresillian North Mothercraft Training Home, Willoughby, New South Wales: Honorary Medical Officer.

Yeoval Subsidised Doctors' Committee, Yeoval, New South Wales: Medical Officer.

Medical Appointments: Important Notice.

Medical Practitioners are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCHES.	APPOINTMENTS.
New South Wales: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
Victorian: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
Queensland: Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17.	Brisbane Associate Friendly Societies' Medical Institute. Proserpine District Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
South Australian: Secretary, 178, North Terrace, Adelaide.	All Lodge appointments in South Australia. All Contract Practice Appointments in South Australia.
Western Australian: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.

Editorial Notices.

Manuscripts forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to The Medical Journal of Australia alone, unless the contrary be stated.

All communications should be addressed to the Editor, The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, The Medical Journal of Australia, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognise any claim arising out of non-receipt of journals unless such a notification is received within one month.

Subscription Rates.—Medical students and others not receiving The Medical Journal of Australia in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £2 for Australia and £2 5s. abroad *per annum* payable in advance.